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CONGENITAL WEBBING OF THE NECK

DONALD W. MACCOLLUM, M.D.*

BOSTON

APPROXIMATELY 20 patients with congenital webs of skin extending from the mastoid process to the acromial process have been described in medical literature since Kobylinski[1] first reported the condition in 1883. These cases have been listed under such terms as webbed neck, pterygium colli, cervical patagium and *Flughautbildung*. The most recent paper of Chandler's[2] in which the literature has been reviewed makes it evident that nearly every author agrees that this anomaly represents an insufficiency of skin over the lateral surface of the neck, and each has offered a different explanation of its cause. This report adds one more explanation, in an attempt to clarify the situation by advancing a theory for the embryologic development of the webs. The fundamentals of this conception are based on a study of 4 patients with this malformation and of several fetuses of varying ages. A typical case is mentioned and the result of its plastic correction is illustrated.

EMBRYOLOGY

During the early weeks of fetal life the neck is difficult to distinguish from either the head or the shoulders, as the diameters of all three structures are very nearly the same. As the branchial arches grow ventrally to form the lower face and anterior portion of the neck, and as the limb buds begin to develop, the neck becomes a definitely recognizable structure. Its actual length, however, is almost negligible, as the cervical flexure of the fetus places the chin against the thorax, and that portion of the head which is to be the mastoid process remains almost continuous with the shoulder. As the fetus continues to develop, the head grows more rapidly than the rest of the body so that in the second or third month of pregnancy it has become one fourth to one third wider than the shoulder girdle. Observations made at this period reveal that the neck is quite long on its dorsal surface because of the cervical flexure. It is found to be even longer on the ventral surface because of the medial ingrowing of the branchial arches. It is to be particularly noted that there is very little length to the neck on both its lateral surfaces, and that the region of the mastoid process is likely to be either lateral to or in a direct vertical line with the region of the acromial process. If at this time there is a failure of normal development, it is possible for the skin over the lateral surfaces of the neck to remain shortened. As the body grows and the shoulders assume their normal width, the skin will be even more deficient, so that tight bands or webs will form between the acromion and mastoid, the two points which were so closely approximated in early fetal life. The fact that this anomaly is always bilateral helps to substantiate this theory of development.

This maldevelopment may be associated with other anomalies. In some instances webs similar to those in the neck exist at the inner canthi, or in the antecubital space, popliteal space or groin. A case of this kind has been seen at the Children's Hospital in which webs existed in all the sites mentioned. The patient also had a cleft palate, which was repaired, but the correction of the webs was not allowed by the parents. The embryology of these multiple webs may be explained on the same structural hypothesis as are those of the neck. In another case seen at the Children's Hospital the patient had a lymphangiectasis of the foot, which was treated successfully with multiple endothermy coagulations and excisions. The neck bands were not so marked as those shown in Figures 1-4, so the parents wished the repair of these postponed until the child was older. In many of the cases described in the literature the cervical spine is deformed, the most frequent phenomena being either abnormalities of the vertebral bodies or an anomalous vertebra. Some of the patients having vertebral aberrations may appear to have

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these webs, when actually the condition is one of reflection of the normal skin over the distorted muscle and fascial layers beneath. The latter cases should not be confused with those of true skin webs.

Figure 1.

Figure 2.

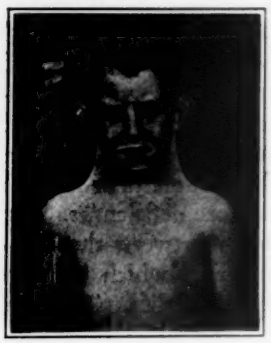

Figure 3.

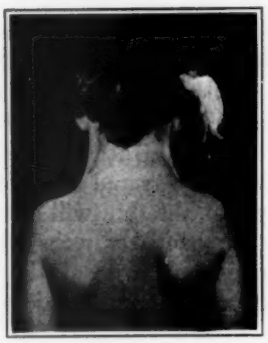

Figure 4.

A girl of eleven with webs of the neck present since birth. Figures 1 and 2 show the extent of the webs—note that the hair, even though shaved in preparation for operation, grows down the posterior aspect of each web. Figures 3 and 4 show the unsightly appearance on anteroposterior and posteroanterior views.

Some observers have attributed these anomalies to amniotic adhesions or bands (Ballantyne[3]) and others to endocrine dysfunction (Nageotte-Wilbouchevitch[4]), while still others believe that the structures represent rare atavistic manifestations. To quote Ballantyne:

> Bland-Sutton (*Evolution and Disease*, p. 143, 1890) places these web-like expansions among the instances of spurious atavism, and refuses to see in them any attempt to reproduce in the human subject the parachute of flying mammals or the wings of birds. I quite agree with him. Possibly the patagium may be due to amniotic pressure which keeps adjacent parts of the body abnormally in contact during development; but it must be admitted that there is a degree of mystery about it in whatever part of the body it may be found. To regard it as a "spontaneous variation or sport" (Bland-Sutton) does not throw much light upon it.

Neither of these explanations seems to throw much light on the subject. Although the cause of developmental arrests in such cases is not understood any more than it is in those with other congenital anomalies, the theory advanced in this communication seems logical since it follows the basic principles involved in the formation of the neck.

PATHOLOGY

Unfortunately very little is known of the microscopic pathology of webs. So far as it can be ascertained, De Bruin[5] is the only observer who has had the opportunity of carefully studying these structures. He has reported that sections taken from the webs of a patient at autopsy showed muscle directly beneath the skin, forming with the superficial cervical fascia the main structures of the folds. This suggested that an abnormal distribution of the platysma fibers was the etiologic factor in the formation of these bands. In 2 cases treated at the Children's Hospital it was evident on gross examination that the bands were

Figure 5.

Figure 6.

Figure 7.

Figure 8.

Same girl after operation. Figure 5 shows the scars of the two flaps on the right side, two weeks after operation. Figure 6 shows the scar of the Z flaps on the left side, four weeks after operation. Figures 7 and 8 show the results of the plastic correction four months after the last operation.

made up of skin and subcutaneous tissue only. No material was taken for microscopic study. The subcutaneous tissue seemed unusually thick and fibrous but contained no muscle bundles. In each case the cervical fascia and platysma muscle were normal and were easily freed from the skin by finger dissection. There were no bands of fibrous tissue or muscle extending from the deeper layers to the skin. The findings in these cases do not suggest a fundamental anomaly of the muscle as the causative agent of the webs. It must be recognized, however, that the presence of muscle in these folds in no way negates the theory of development which has been proposed. In people who do not have such webs it is known that the platysma may have an abnormally broad origin with fibers inserting into the mastoid process. If this were the case in a patient who developed webs, it would be possible for these anomalous fibers to remain as shortened as the skin, and therefore to form an integral part of the fold.

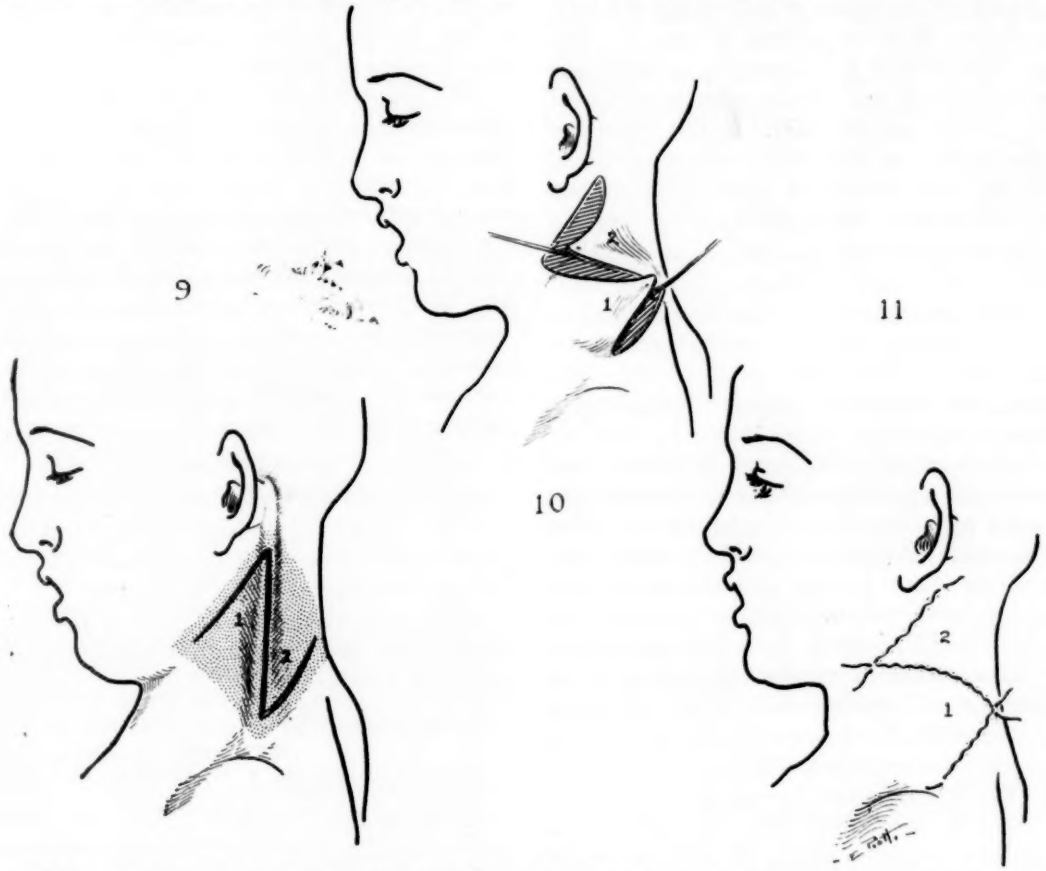

Figure 9 shows the outline of the Z incision. Figure 10 shows the transposition of the two flaps with the release of the web. Figure 11 shows the completed operation: the skin edges are approximated with three continuous subcuticular sutures of No. 00000 Dermic.

TREATMENT

Repair of these skin folds by means of the Z type of transposed flap is not new (Chandler[2]), but there are a few precautions and suggestions which are of interest to record.

(1) A larger Z must be outlined for the correction of these folds than would normally be made for web contractures following injury, both because of the extent of the webs and because of the apparent inelasticity of the tissue.

(2) The Z should be formed so that the hairiest triangular flap will be transposed beneath the ear, allowing the most hairless flap to be carried down to form the lower lateral portion of the neck. This will avoid the cosmetic objection of having hair grow down the back of the neck, as would be caused by a Z incision in the opposite direction (Figs. 9-11).

(3) Prior to operation, the lines of the incision should be marked out on *both* sides of the neck. The greatest emphasis must be placed upon making these incisions exactly alike on each side. In order to do this properly, calipers and protractors are needed. The length of the planned incisions and the angles between them must be incorporated in the patient's hospital record so that when the marks have been obliterated by the preparation of

the field and the draping of the patient, the same Z incision may be repeated. If this is not done, an asymmetrical neck will result.

(4) Only one web should be corrected at a time. It is difficult to ensure proper and even pressure on both sides of the neck if both webs are repaired at the same operation. For this reason also, the recording of the plan of the incisions is important, as the operator may forget the exact measurements after an interval of two or three weeks. Furthermore, it is necessary to undermine the entire neck on one side in order to relieve all possible tension on the skin. If this procedure were carried out on both sides at once the entire skin of the neck would be lifted from its bed, thereby endangering the viability of the flaps.

(5) Hemostasis must be absolute so that there will be no thickening of the flap from an unresolved hematoma beneath it. Bleeding is best controlled by crushing the ends of the vessels with arterial clamps rather than by ligatures. This minimizes the reaction to foreign material under the flaps.

(6) All existing tension must be placed upon sutures in the subcutaneous layers. Suture material should preferably be of No. 0000 plain catgut. If silk is employed it is wise to use the finest white silk available so as to prevent the possibility of black spots from showing through the scar at a later time. The skin should be closed by a fine, continuous, subcuticular suture to avoid cross marks. If interrupted sutures are used they should be of fine silk of No. 00000 Dermic and should be removed in forty-eight or seventy-two hours.

(7) The dressing must be applied so that even, firm pressure is exerted over the entire field, that is, both triangles of the Z, and the undermined portions of the neck not included in the flaps. This result is best obtained by "shingling" the neck with several layers of 1-inch strips of gauze. These strips are held in place by Elastinett, Elastoplast and Ace bandage. In children it is difficult to prevent movement of the neck, but if this form of bandage is applied heavily enough it will serve as a most effective splint. In order to prevent any possible tension on the skin, a meshed tape should be applied over the incision and is held in place by a sticky varnish. If any sudden movement of the neck is made, the tension is then exerted on the tape, rather than on the sutured edges of the skin.

(8) The treatment after the sutures are removed consists in neck massage twice daily, beginning on the fourteenth day and continuing for at least six months. The direction of the line of massage must always correspond to that of the flap, for example, toward the apex of the triangle so that all movement in the upper part of the neck will be directed from behind forward, while all movement in the lower neck is directed in the opposite direction. Stretching and rotation exercises are also helpful to gain normal mobility and contour of the neck.

SUMMARY

Based upon a study of 4 cases and several fetuses, a theory of the embryologic development of congenital webs of the neck (pterygium colli, cervical patagia, *Flughautbildung*) is proposed.

Suggestions for the plastic repair of this anomaly are outlined and illustrated as already applied to a typical case.

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THE PROBLEM OF CONGENITAL SYPHILIS IN BOSTON

A Two-Year Survey of a Clinic

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BOSTON

THE importance of the early recognition and treatment of congenital syphilis is well established. Criteria for determining the presence of or freedom from the disease have been clarified in recent years. These criteria depend in most instances on repeated examinations during infancy, inasmuch as outspoken clinical signs of congenital syphilis may not be evident at birth. To secure the return of an apparently healthy, outwardly unmarked infant to a clinic calls for an unusually intelligent or co-operative mother or the urgent prompting of a social worker. The present study represents a survey, during 1935 and 1936, of the follow-up system affecting the infants born at a large maternity hospital in Boston.

Acquired syphilis is on the decline in Massachusetts.[1] Judging by the experience of Madsen[2] in Denmark, the incidence of congenital syphilis presumably has followed the same trend.[3] So long as the disease exists, however, even though it is diminishing, a definite social responsibility must be recognized toward infants born of syphilitic mothers. The relative infrequency of congenital syphilis cannot be accepted as an excuse for haphazard methods for recognizing the disease in its earliest stages. The efficacy of modern treatment adds to this responsibility.

At the Boston Lying-in Hospital, the general prenatal care of the women is excellent and a blood Hinton test for syphilis is obtained on the first visit of each expectant mother. Those whose tests are positive are referred to other clinics in the city or to local physicians for specific treatment. This step involves the delay of a week or more and results in some division of responsibility.

After their discharge from the maternity hospital, the syphilitic mothers do not always return to the clinics where they were treated during their pregnancy. Although the present understanding between the majority of clinics in Boston is that the clinic treating the mother shall also be responsible for her infant, these clinics are not as a rule aware of the existence of the infant, unless the mother herself informs them.

During the years 1935 and 1936, 125 women with positive blood tests, or 1.7 per cent of the total number of patients delivered during these two years, applied at the Boston Lying-in Hospital for prenatal care — 64 in 1935 and 61 in 1936. Of these, 106 were actually delivered under the auspices of this hospital, either on the wards or at home. Eleven cases were eliminated from this number, principally because it was impossible to obtain subsequent information about them. This left 95 syphilitic women whose infants comprised the basis of the study.

For their antisyphilitic treatment during pregnancy, these mothers were referred to widely scattered clinics. Over half went to the Massachusetts General Hospital, and about one quarter to the Boston City Hospital. The Boston Dispensary, the Peter Bent Brigham Hospital, the Massachusetts Memorial Hospitals, the Cambridge City Hospital, the Cambridge Hospital and the Boston Psychopathic Hospital treated the remainder. The age group was that of most women in the child-bearing period. There were two sets of twins, which makes 97 infants in all. Three mothers had infants in both years and were counted twice. Table 1 shows the original diagnoses found on the records of the women at the clinics attended for specific treatment.

Table 1. *Tabulation of the Diagnoses.*

DIAGNOSIS	NO. OF CASES
Tertiary, latent or asymptomatic syphilis	61
Congenital syphilis	20
Secondary syphilis*	8
Primary syphilis*	3
"No disease"	2
Not examined	1
Total	95

*For the purposes of this study, all but 2 of the cases of primary and secondary syphilis may be considered latent, since the infection was of some years' standing.

The marital history of these women was of interest in view of the accepted principle that all possible contacts with a case of syphilis should be investigated. So far as could be discovered from the records, which of course may not be complete, 40 husbands were examined serologically and 24 gave positive reactions. There had been recorded 254 previous pregnancies, the outcomes of which were varied (Table 2). It is especially significant that 125 (68 per cent) of the 183 supposedly normal children had never had a blood test.

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Of the 95 pregnancies included in the 1935-1936 period, 2 resulted in abortion and 2 in stillbirth. Three pregnancies resulted in infants in whom congenital syphilis was recognized either at birth or within the first two weeks. Two more infants were found to have congenital syphilis as the result of subsequent examinations, making a total of 5 born alive in whom a diagnosis of specific in-

Table 2. *Tabulation of Results of Previous Pregnancies.*

DIAGNOSIS	NO. HAVING ONE	NO. HAVING TWO	NO. HAVING THREE	TOTAL PREGNANCIES
Abortion	0	0	0	0
Miscarriage	19	3	0	25
Stillbirth	11	2	2	21
Premature birth	1	1	0	3
Recognized congenital syphilis	10	3	2	22
Normal infant remainder				183
Total				254

fection was definitely established during the period of study.

Eight of the 35 infants born at home of syphilitic mothers had tests on blood specimens from the umbilical cord, 5 were admitted to the maternity hospital for observation, and the remaining 22 were not examined serologically during the neonatal period.

Most of the 62 infants born in the hospital received more careful scrutiny. Besides a careful physical examination, arrangements were made for each infant to have x-rays of the long bones, a blood Hinton test (and sometimes a Wassermann as well), and two or more Davies-Hinton[4] tests. Occasionally a specimen of blood from the umbilical cord was obtained for a Hinton test. The criteria for making the diagnosis of congenital syphilis will not be discussed here, but it may be stated that once the diagnosis was established, the infant was immediately transferred to another hospital for treatment.

The nearby Infants' and Children's hospitals accepted 36 of the 93 living infants for observation or treatment. This large proportion was due to the expressed preference of the mothers or to the fact that in the first few months of the study the infants were directed there on discharge from the maternity hospital. The follow-up schedule at the Infants' and Children's hospitals consisted of periodic physical examinations and blood tests by either the regular Hinton or the Davies-Hinton method at the approximate ages of six weeks, three months and one year. The intervals were sometimes shortened for special reasons, but an effort was made to avoid unnecessary visits. X-rays of the long bones were taken when indicated. At some clinics, such as those of the Massachusetts General Hospital and the Boston Dispensary, the plan of follow-up examination was similar; at others, the schedule was left to the individual physician and no general policy had been formulated up to the end of 1936.

Although efforts were redoubled at the beginning of 1935 to secure the re-examination of all infants whose mothers had had syphilis, 32 had apparently not been seen by any physician, even for one visit, up to May 1, 1937, four months after the last infant was admitted to the survey. Many of those examined did not have the benefit of a blood test.

The amount of previous treatment received by the syphilitic mothers of the 32 infants who were examined after leaving the maternity hospital forecast slight protection of these infants from infection, unless one takes into consideration the interval since the initial infection of the mother. This time relation could not in most cases be determined even approximately from the records, but the amount of specific treatment recorded showed that 11 of the 32 mothers had had no treatment during this pregnancy and 17 had had what might be termed minimal or wholly inadequate treatment, according to modern standards.[5] Fourteen of these women started their treatment after the fifth month of pregnancy, which is considered too late for reasonable safety, even under intensive treatment.

The 5 pregnancies that resulted in recognized congenital syphilis and the 4 that resulted in miscarriages or stillbirths illustrate the parallelism between treatment and the outcome of pregnancy. Only 1 of the mothers of the infants who were found to have congenital syphilis had had more than minimal treatment during this pregnancy, and her treatment had been started after the fifth month. She had previously had no treatment of any kind, and her history disclosed a miscarriage, 2 children with congenital syphilis, and 1 infant that died at the age of fifteen days of an undetermined cause. None of the 4 mothers whose pregnancies resulted in stillbirths or miscarriages had had more than minimal treatment at any time.

It is apparent that the previous maternity record of the 95 syphilitic women in the group studied was far from reassuring. They had had at least 46 miscarriages and stillbirths and 22 children with recognized congenital syphilis, and yet 68 per cent of the remaining children had never had the benefit of a blood test, so far as could be discovered from the records. During the two years of the survey, a special effort was made, with the follow-up facilities at hand, to secure the re-examination of the infants born in that period of syphilitic mothers. Five cases of congenital syphilis were detected, 2 as the result of examinations after leaving the maternity hospital. However, 32 infants, or 34 per cent, had not had even one examination after

the first two weeks of life, although the mothers of the majority of these received less than adequate treatment during pregnancy.

The investigators were impressed with the fact that some of the clinics in metropolitan Boston, whose staff members were aware of the importance of keeping the infants under observation, appeared to lack the necessary social-service facilities for bringing about the desired examinations. There was considerable confusion as to where responsibility for the infants lay. A few of the clinics had good intentions but no definite policy and the matter was left largely to chance.

An important step forward has been taken, since the completion of this survey, toward remedying some of the defects pointed out above in the arrangements for handling these patients. Through the Massachusetts Department of Public Health, a special social worker has recently been placed at the disposal of the hospitals of Boston, whose duties are to co-ordinate social effort in this field, to act as a clearing-house for information, to promote the early treatment of pregnant syphilitic women and to secure the return of their infants to clinics or to private physicians for careful examination. One might add the hope that these clinics will adopt, by common consent, a uniform policy regarding the details of the follow-up examinations of infants born of syphilitic mothers. This policy should be in harmony with the newer knowledge regarding the criteria for the diagnosis and exclusion of congenital syphilis.[6]

SUMMARY

A survey of the background of a group of infants born in Boston of syphilitic mothers during 1935 and 1936 is presented. Their status is discussed, and the defects in the follow-up arrangements are pointed out, together with a remedy which promises better co-ordination of effort in the future.

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ACCIDENTAL INJURY TO THE HEART BY NEEDLE PUNCTURE

A Report of Four Cases

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IT is recognized that severe or even fatal damage to the heart may occur in attempted intracardiac injection of drugs or attempted paracentesis for the removal of effusion into the pericardial sac.[3] Since such accidents are rarely reported, the potential danger of these procedures is not sufficiently emphasized. Furthermore, the experience of a single individual with these methods of therapy will be limited because they are relatively infrequent. For these reasons it seems worth while to report the following cases of severe accidental injury to the heart as a result of these two forms of therapy. They were discovered in reading 9626 consecutive protocols of necropsies performed at the Boston City Hospital from 1906 through 1936. The first 2 had fairly complete records, while clinical data on the last 2 were meager.

CASE REPORTS

Case 1. J. S., a 4-year-old, white, American boy, was admitted to the hospital with evidence of scarlet fever, acute septic pharyngitis and cervical adenitis. The heart was not enlarged, the sounds were of good quality, and the rhythm was normal. The blood pressure was 115/85. Three weeks after onset the convalescence was interrupted by the sudden appearance of vomiting and respiratory difficulty. Examination of the urine revealed a large amount of albumin, red cells and casts. Vomiting continued and on the second day the blood pressure had risen to 140/106. An acetone odor was noticed on the breath. The cardiac rhythm was regular, but a systolic murmur was heard at the apex. Five days later the blood pressure was only 125/80. A gallop rhythm was detected and respirations rose to 60 per minute. It was found that the left border of cardiac dullness extended almost to the anterior axillary line, and a diminution of breath sounds was noted in the lower half of the left chest posteriorly. The next day the blood pressure was 140/122 and the liver was tender and palpable at the level of the umbilicus.

At this juncture a pericardial tap was attempted. It was recorded that the needle was inserted 2 cm. to the left of the ensiform and 5 cc. of bloody fluid obtained. Following this procedure the patient was orthopneic and very cyanotic. At times the pulse was not obtainable. The liver and heart were unchanged. In spite of magnesium sulfate given intramuscularly and clyses of 5 per cent glucose, vomiting continued and the general condition remained bad.

On the day following the first pericardial tap, another was essayed; the needle was inserted in the 4th left inter-

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space 1 cm. inside the nipple line and 15 cc. of blood was obtained. A few minutes later the patient suddenly became pulseless but continued to gasp for 5 minutes after the heart had stopped. Artificial respiration and intracardiac adrenalin were used without success.

At autopsy, a small bilateral pleural effusion was found. The pericardium, showing three needle wounds, was distended with 200 cc. of liquid blood and clots. Three puncture wounds appeared in the anterior wall of the right ventricle. Two of these were 1½ and 2 cm. from the apex and communicated directly with the ventricular cavity from which blood could be expressed by squeezing the heart in situ. The third rent was located 4 cm. from the apex near the interventricular septum but did not communicate with the interior of the ventricle. The valves, endocardium and coronary arteries were normal and the heart weighed 100 gm. The kidneys revealed gross and microscopic lesions of acute nephritis.

Comment. Whether a pericardial effusion was present in this case is not clear, but the enlargement of cardiac outline may have resulted from dilatation alone. Death was typically that of cardiac standstill. The final and futile effort to restore the heart to activity by intracardiac adrenalin is noted.

Case 2. S. G., a 53-year-old, male, Italian shoemaker, was admitted to the hospital 6 months after a sudden attack characterized by dyspnea, weakness and oppression. He was known to suffer from mild diabetes mellitus, which was regulated by diet without insulin. Prior to admission he had had many attacks of cardiac asthma. Physical examination revealed an obese, cyanotic and orthopneic man with temperature 98.7°F., respirations 30 and pulse 130. The heart was enlarged in all directions. The sounds were of poor quality and could be heard best at the base. There was a diastolic gallop rhythm. The pulse was of poor quality, the peripheral arteries thickened, and the blood pressure 106/90. The liver was palpable 4 fingerbreadths below the costal margin. Shifting dullness was noted in the abdomen, and marked edema of the legs extended well above the knees. An electrocardiogram revealed a normal sinus rhythm; PR interval of 0.22 seconds: Q-R-S interval of 0.08 seconds with T_1 inverted, T_2 diphasic and T_3 upright. The axis was normal, but the amplitude only 4 mm. On the 5th day the heart sounds had improved, and the rate was 96. At times there were sharp attacks of dyspnea lasting 5 minutes. Another electrocardiogram 8 days after admission showed an absence of the Q wave in the chest lead, and the T waves were diphasic in all leads. Two days later the attacks of dyspnea became more severe, and a faint transient friction rub was heard in the 3rd interspace to the left of the sternum. Further widening of the cardiac dullness to both sides was noted, and the blood pressure was 98/88. The next day an x-ray film showed "globular enlargement of the heart and widening of region of the great vessels — pericardial effusion." On the 15th day a pericardial paracentesis was attempted. The needle was introduced into the 4th right interspace near the sternum, and 160 cc. of straw-colored fluid removed. This was followed by moderate relief. Three days later the symptoms had become aggravated and a second tap was tried. The site is not recorded but 10 cc. of pure blood was removed. The following day the pulse pressure was only 6 or 8 mm. Orthopnea, cyanosis and edema progressed. The temperature rose to 104.6°F., the pulse to 120 and respirations to 45. A third pericardial tap was begun but was discontinued immediately upon entering the pericardial cavity when frank blood was encountered. The patient finally died on the 22nd day after admission, 4 days after the right ventricle was punctured.

At autopsy (limited to heart and pericardium), the pericardial cavity contained 200 cc. of blood and some clots. The greatly dilated heart weighed 560 gm. In the anterior aspect of the right ventricle near the septum was an irregular puncture wound 3 mm. in diameter, surrounded by organizing fibrin. A probe could be passed through this into the ventricle. Another wound 4 cm. lateral to this penetrated only about half the hypertrophied part of the ventricular wall. There were several pearl-gray granules one third to one half the size of a pinhead on the right auricle. A bulging old scar included the anterior aspect of both ventricles (4 cm. of the left and 2 cm. of the right). The tear was in the aneurysmal bulge. The lumen of the anterior descending branch of the left coronary artery was reduced to 1 mm., and there was complete occlusion of the branch leading to the scar. Small, friable mural thrombi were found in both ventricles in this area. Calcification of the aortic valve was present.

Comment. This patient had had a "painless" infarct of the heart six months before admission. It had been followed by congestive failure. When the friction rub was heard and clinical evidence of widening of the cardiac borders was noted, the x-ray was considered quite typical of pericardial effusion. When the straw-colored fluid was removed, this diagnosis was verified. Subsequently it was concluded that the increase in severity of the symptoms was due to an increase in the pericardial effusion. The second tap penetrated into the ventricle and the slowly developing hemopericardium increased the burden of the already seriously damaged heart. The terminal rise in fever, pulse and respirations was probably due in part to the blood in the pericardium. A similar state may occur in stab wounds of the heart. It was not suspected clinically that this patient had a ventricular aneurysm. Various physical signs which occur in cardiac aneurysm are not pathognomonic,[5] and if x-ray evidence is not clear-cut, the diagnosis cannot be made. It should be thought of in cases of enlarged heart where coronary artery disease is present and the problem of effusion presents itself.

Case 3. J. H., a 28-year-old, white, male, American stenographer, was admitted complaining of a swelling in the lower anterior aspect of the neck, of 4 days' duration. This was a recurrence of a similar condition which had appeared 3 months earlier with rapidly developing swelling, cough, dysphagia, pain, fever and chills. Physical examination revealed a well-developed and nourished young man with a red, tender, slightly fluctuant area in the anterior part of the neck in the region of the thyroid gland. This was very indurated around the margins. The pulse, temperature and leukocyte count were elevated. No other abnormality was noted in the physical examination or laboratory work. It was decided to do an emergency tracheotomy because of the beginning obstruction to respiration. Induction of ether anesthesia was uneventful,

but as soon as the incision was made respiration became labored and cyanosis appeared. When a pus pocket was encountered and evacuated, respirations and pulse ceased. The tracheotomy was immediately completed, and a carbon-dioxide and oxygen mixture was given through the tube, intracardiac adrenalin was given, and artificial respiration was instituted and continued for 20 minutes. Death was recorded as due to anesthesia.

The only pertinent part of the autopsy concerns the heart and pericardium. The heart weighed 400 gm. There was 175 cc. of blood in the pericardial sac. There were two small puncture wounds in the anterior aspect of the left ventricle, one of which had punctured a coronary artery. Blood was readily expressed from the wound.

Case 4. F. E., a 57-year-old, white, unemployed, American male, was admitted complaining of episodes of right-upper-quadrant pain, chills, fever, vomiting and intermittent jaundice. The first of these attacks had occurred 5 months previously. Pertinent facts in the physical examination included moderate obesity, slight jaundice, tenderness and spasm in the right upper quadrant of the abdomen. There was a temperature of 101°F.; x-ray studies indicated a functionless gall bladder, and a diagnosis of gallstones was made. An operation was performed under spinal anesthesia, which had to be reinforced by gas and ether. An empyema of the gall bladder was found. While the gall bladder was being fully exposed, respirations and pulse suddenly failed. Artificial respiration and intracardiac adrenalin were tried without avail.

At autopsy, the pericardium was distended with 200 cc. of blood. There was slight cardiac hypertrophy. A traumatic puncture wound of the heart was present but the site was not mentioned. Blood could be expressed from the cardiac laceration by moderate pressure.

Comment. These 2 cases add concrete evidence to the belief which was set forth in an editorial[2] in 1930 condemning the practice of attempting to resuscitate every asystolic heart by intracardiac injections. While it is probable that the lacerations of the heart in these cases were not the cause of death, it is certain that recovery was interfered with rather than facilitated. Though such accidents must be rare, their potential danger is manifest. In a careful appraisal of intracardiac therapy Hyman[4] concluded that the right auricle approached from the third right interspace was the site of election in attempting to revive the heart. In addition he gave evidence that it was mechanical stimulation of the auricular wall, rather than the drug injected, that was the important factor. A needle wound in the auricle is not so potentially dangerous as one in a coronary artery or vein.

These cases suggest that intracardiac injection of adrenalin and paracentesis of the pericardium for effusion are sources of grave danger. No data are available concerning the incidence of damage to the heart from such procedures. In spite of the fact that these accidents are relatively rare, knowledge of such disasters is a warning of the danger. The common teaching that pericardial paracentesis is a safe procedure[7] is justified only if these points are kept in mind. In the 2 cases reported above no attempt was made to remove the pericardial fluid from behind, as recommended by Conner[1] and others,[6, 8] where the danger of injury to the heart is minimal. It should be remembered that wherever the needle be introduced it is important not to manipulate it in situ. Even with this precaution, the change of position of the heart with each contraction and relaxation may cause laceration if the needle impinges thereon. Probing to reach fluid increases the hazard.

SUMMARY

Four cases of severe damage to the heart from attempts at therapy are reported and the dangers of these procedures are discussed.

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THE DANGERS OF TUBERCULOSIS IN CHILDHOOD

A Study of Hospital Mortality

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THIS study represents an attempt to discover facts relative to the mortality from tuberculosis among infants and children, and to determine what constitutes intelligent management of the disease in these age groups.

Obviously, the most desirable statistics would show the percentage of children in any group who become diseased, and the percentage of diseased children whose illness terminates in death. Statistics of this kind presuppose ability to determine with certainty the presence of active tuberculous infection, and to state how recently it has begun. Such statements may be definitely made in infants, but in older children they are much more difficult. In the latter case it is usually impossible to state how long infection has existed; the roentgenologic findings of mild involvement of the different regional systems are not highly specific, and the clinical manifestations are even less helpful. More difficult still is the question of ultimate recovery or ultimate death. In order to determine with finality what percentage of children who are infected with the tubercle bacillus eventually succumb, it would be necessary to follow patients into adult life — in fact to death from whatever cause.

Perhaps the greatest difficulty in obtaining such ideal statistics from hospital experience arises from the fact that most tuberculous patients are admitted in an advanced or fatal stage of the disease. Tuberculous conditions in infants and children are accompanied by so few symptoms that mild or early stages are usually brought to light only by energetic case-finding methods. As a result, hospital figures tend to be overweighted on the side of mortality and perhaps to be insufficiently representative of morbidity.

We have come to suspect, however, that the records of a large series of children dying from tuberculosis in a pediatric clinic would reveal the relative dangers of death in the different periods of childhood, and would indicate what pathologic processes are most to be feared at various ages. The dangers of tuberculosis in infancy are becoming increasingly well understood through a number of careful studies.[1] But with regard to the older child one finds less definite information in the literature as to what outcome may be expected and what immediate dangers must be envisaged. Thus, among patients of this age group referred to a tuberculosis clinic or to a general pediatric dispensary, one sees no uniformity of approach by referring physicians. For example, a child of ten who reacts to tuberculin and whose mediastinal shadow shows a slight widening by roentgenogram may come to the clinic with recommendation for immediate sanatorium placement, while the parents of a child with identical symptoms may have been told that his condition is more or less normal and needs no further attention. Because of the lack of data available for this age group, we have concentrated our study upon the findings in older children.

The records of 345 patients have been examined. This number represents all the deaths due to tuberculosis in the Infants' and the Children's hospitals from 1923 through 1937. Of these deaths, 200 occurred in the Infants' Hospital. This institution admits patients of less than two years of age. During the same period there was a total of 11,787 admissions. Thus there was 1 death from tuberculosis for every 59 infants admitted. The remaining 145 patients were seen in the Children's Hospital, which admits patients of two to twelve years of age. There were 13,772 general admissions in this group, and for every 95 admissions there was 1 death from tuberculosis. Records of children succumbing to such conditions as amyloid disease in the presence of tuberculosis have not been included, as it was desired to appraise as exactly as possible the dangers of tuberculosis itself. Necropsy examinations were made on 178 patients, and the protocols have been studied with especial care. Among 167 patients upon whom necropsy was not permitted, no record has been included unless the diagnosis was definitely established — usually by bacteriologic examination or by the roentgenologic appearance of miliary tuberculosis.

Obviously the upper age limit of twelve prevents this material from extending into the period of fatal tuberculosis occurring in the teens. We urge that the findings be interpreted with this in mind. Also, it should again be emphasized that we do not offer any direct information concerning the prognosis of the infected child as he passes into this critical succeeding period. Our main purpose has been to determine by what pathologic processes

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and with what frequency tuberculosis causes the deaths of children below the age of twelve.

Table 1. *Deaths from Tuberculosis in the Infants' and the Children's Hospitals, 1923-1938.*

YEAR	AGE IN YEARS												TOTALS
	0-1	1	2	3	4	5	6	7	8	9	10	11	
1923	6	6	3	3		1		1	1				21
1924	16	15	6	1	3	2	1	2					46
1925	11	13	7	3	2	2	1	1					40
1926	12	12	5	3	4	2		1	1				40
1927	3	10	4	2	2		1	1			1	1	25
1928	6	8	4	1	1					1			21
1929	8	9	7		1	3	1	2	1			2	34
1930	4	10	3	4	1	3	1	1					27
1931	6	3	5	4				1	1				20
1932	5	2	4	2	1		1			1			16
1933	3	6	2	1						1			13
1934	3	8	2		1							1	15
1935	2	2	1	3		2			1		1		12
1936	1	3	2					1					7
1937	2	5			1								8
Totals	88	112	55	27	17	15	6	11	5	3	2	4	345

The first fact which appears from a tabulation of the data (Table 1 and Fig. 1) is that the mortality from tuberculosis has diminished considerably during this comparatively short period. The decline has been commented upon by another author[2] and is shown also in Table 2, in which the latest available figures for Massachusetts are presented.[3] It is gratifying to note that while the state records show a steady decline in tuberculosis mortality at most ages, the decline is sharpest for the early ages of life, which holds true also for the hospital figures.

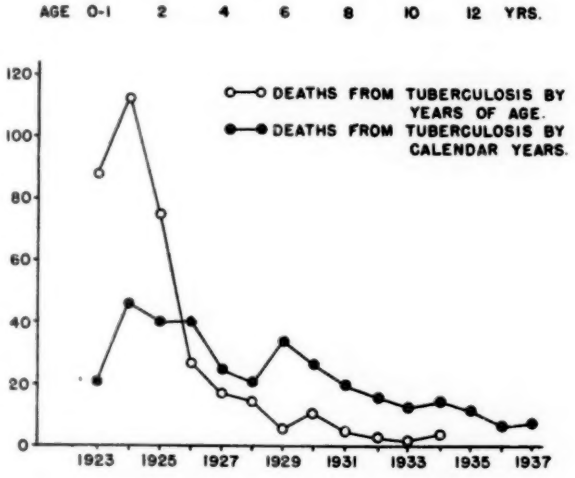

Figure 1. *Distribution of 345 deaths from tuberculosis according to age and according to calendar years.*

A second point which becomes apparent from the data is that the first two years of life furnish the majority of deaths in the age period presented. This widely recognized fact, which also appears in the Massachusetts statistics, is more graphically demonstrated in Figure 1, which shows the number of deaths in the series reported here at each year of age. As has been stated, it is not so much the peak of mortality in infancy as the smaller number of deaths in later childhood that has been of chief interest in this study. The recognized seriousness of infantile tuberculosis has caused a proper amount of apprehension and investigation, with the result that methods of prevention and treatment have produced the marked decrease in its mortality mentioned in the preceding paragraph.

Table 3. *Mortality in Three Age Periods.*

Group 1		Group 2		Group 3	
AGE	DEATHS	AGE	DEATHS	AGE	DEATHS
0-1	88	2	55	7	11
1-2	112	3	27	8	5
		4	17	9	3
		5	15	10	2
		6	6	11	4
Totals	200		120		25

For the purpose of this communication it has been convenient to classify patients according to age, as shown in Table 3. This places something over half the cases in Group 1, the period of infancy. More than one third fall into Group 2, which represents the next five years, and less than one tenth are comprised in Group 3, the period from seven to twelve years. The shape of the curve in Figure 1 indicates that children in the earlier years of Group 2 may be considered much as are the infants of Group 1, while those in the later ages of Group 2 may be expected to conform to the observations made from Group 3.

Table 2. *Deaths from Tuberculosis in Massachusetts, 1922-1936.*

YEAR	AGE IN YEARS														TOTALS
	0-1	1	2	3	4	5-9	10-14	15-19	20-29	30-39	40-49	50-59	60-69	70+	
1922	102	98	38	30	17	56	71	242	914	788	595	428	244	112	3735
1923	94	76	44	31	25	77	76	240	917	738	564	404	213	93	3592
1924	90	99	37	32	28	51	64	243	874	703	565	396	248	99	3529
1925	88	96	43	23	24	45	73	247	826	680	572	411	244	87	3459
1926	86	88	49	25	26	58	48	247	805	700	581	416	273	113	3515
1927	66	69	29	19	8	49	60	244	778	667	495	471	426	101	3482
1928	56	68	34	26	16	43	39	243	703	650	567	319	265	100	3129
1929	42	42	30	10	8	40	54	201	663	637	484	364	245	102	2922
1930	26	46	18	14	14	47	36	182	682	612	480	371	206	100	2834
1931	31	33	20	12	14	30	45	136	546	525	508	318	223	113	2554
1932	34	27	19	10	8	22	29	120	489	468	416	327	216	114	2299
1933	18	25	19	15	3	20	22	135	458	458	417	346	230	115	2281
1934	13	24	7	8	6	22	35	108	351	415	383	317	223	101	2013
1935	7	12	10	5	6	14	22	106	373	394	405	292	202	112	1960
1936	14	11	16	6	5	14	19	72	347	349	338	324	251	110	1876
Totals	767	814	413	266	208	588	693	2766	9726	8784	7370	5504	3709	1572	43180

In the fifteen years covered, there were 25 deaths between the seventh and twelfth birthdays, as against 200 in the first two years of life. To determine the facts responsible for this small number of deaths in Group 3, attention was concentrated on necropsy material. For the three groups necropsy findings were available for 125, 41 and 12 patients respectively. Interest was centered on the type of primary lesion demonstrable, the form of tuberculosis immediately responsible for death, and the presence of associated abdominal or skeletal tuberculosis. Patients in whom only a few scattered tubercles occurred in the spleen or liver are not included in the figures for miliary tuberculosis. A tabulation of necropsy findings is presented in Table 4. While too great importance should not be placed upon the small number of cases in Group 3, the trend of percentages for most pathologic categories through the three groups indicates that those in the final column are representative and significant.

nodes without lesions in the lungs or hilar nodes. In this case there was chronic tuberculosis of the spine, and death occurred from tuberculous meningitis. Here the primary abdominal focus had probably acted only indirectly as a cause of death, by leading to extension of the tubercle bacillus to the spine and thence finally to the meninges. The number of instances of skeletal tuberculosis found in each group was small, but was proportionately greater with advancing age.

With regard to the immediate cause of death, the comparative frequencies of miliary tuberculosis, meningitis and destructive pulmonary processes are of interest. Miliary tuberculosis, alone or with accompanying tuberculous meningitis, appears as by far the commonest condition of infancy, while in older children it was found in only 3 of the 12 necropsies. In the latter group the majority of deaths were caused by meningitis alone, whereas in infancy a fatal meningitis not associated with a miliary dissemination was rare.

Table 4. *Necropsy Findings in 178 Deaths from Tuberculosis.*

Necropsy Findings	Group 1 (0-2 years, 125 cases)		Group 2 (2-7 years, 41 cases)		Group 3 (7-12 years, 12 cases)	
	Number	Per cent	Number	Per cent	Number	Per cent
State of primary focus in lung or at hilum or both:						
Caseous	81	65	22	54	4	33
Calcified	13	10	10	24	6	50
Not found	3	2.4	4	9.7	1	8.3
Primary in abdomen	19	15.3	3	7.3	1	8.3
Associated bone lesion	2	1.6	2	4.9	2	16.5
Tuberculous condition at death:						
Miliary tuberculosis	24	19.2	2	4.9	2	16.5
Tuberculous meningitis	13	10.4	13	32	9	75
Both miliary tuberculosis and meningitis	85	68	26	63	1	8.3
Pulmonary tuberculosis or tuberculous pneumonia	25	20	0	0	0	0
Cavity	11	8.8	0	0	0	0

Primary foci were usually easily identifiable as such by their gross and microscopic appearance. As was to be expected, they were usually discovered in the lung tissue and in the related lymph nodes. The percentage of primary foci in a state of caseation diminished in succeeding age groups, while, conversely, calcified foci were found more frequently in later childhood. These facts are not surprising, but they illustrate the infrequency of mortality in later childhood from recent primary infections spreading unchecked through the body. In only 8 of the 178 postmortem examinations could a definite primary lesion not be discovered.

In 15 per cent of the infants and 7 per cent of the next older children, evidence of a primary abdominal infection was found. In both these groups such foci had usually developed into active tuberculous peritonitis. This condition was more frequently discovered in the earlier years of this study, and lately has been rarely met with. One child in Group 3 presented calcified mesenteric

No child in the older group had an active or spreading pulmonary process at death. On the other hand, in infancy one fifth of the deaths occurred in the presence of disease designated by the pathologist as active pulmonary tuberculosis or tuberculous pneumonia. A comparison of the percentages of cavities found in infants and in older children supports these observations.

The necropsy findings in 178 patients dying from tuberculosis thus presented the following differences in pathology. In infants, fresh, caseating primary foci were found in most cases; in older children they were less frequently seen. Primary abdominal lesions were commoner in infants than in older children, while lesions of skeletal tuberculosis occurred oftener in the latter group. Miliary tuberculosis, either alone or with tuberculous meningitis, was the rule in infancy, and tuberculous pneumonia or pulmonary tuberculosis was actively present in 20 per cent of infants. Conversely, most of the older children died of menin-

geal disease without miliary dissemination to the rest of the body, and in no older child was active pulmonary disease discovered.

Such evidence as may be drawn from the 13 older children who did not come to autopsy coincides with the findings just summarized. Thus, of these, 9 died of meningitis alone, without roentgenologic evidence of miliary or pulmonary tuberculosis. Three presented the combination of meningeal and miliary disease. The remaining patient died of meningitis in the presence of a tuberculous pleurisy. This was a Chinese boy of ten who was brought to the hospital two weeks after onset of cough and fever, and one day after the appearance of meningeal signs. Roentgenograms showed the presence of a large effusion in the left thorax, above which there was some diffuse pneumonic infiltration. The child died two days later. It is probable that necropsy, had it been allowed in this case, would have shown a spreading tuberculosis of the lung associated with the effusion. Admittedly the data do not extend into adolescence, where the adult type of the disease becomes increasingly significant, but the almost complete absence of death from this type of disease in a fifteen-year series indicates that at ages from two to twelve fatal pulmonary tuberculosis is encountered very rarely and need cause little apprehension.

The combined necropsy and clinical data as to the mortality of tuberculosis in later childhood may be summarized by repeating that of 25 deaths only 1 seemed to be associated with a spreading pulmonary lesion, 6 were due to miliary tuberculosis either alone or in combination with meningitis, and 18 resulted from tuberculous meningitis alone. It is difficult to conceive how meningitis could have arisen in these 18 patients unless from the extension of tuberculous foci in or adjacent to the central nervous system. Although we have not been so successful as were Rich and McCordock[4] in demonstrating such foci, their presence would be a highly reasonable explanation for the sudden appearance of tuberculosis confined to the meninges.

From the foregoing analysis of mortality, certain deductions can be made concerning the proper management of the tuberculosis problem in the ages studied. In infants it seems justifiable to regard fatalities as the result of rapidly progressing and spreading infections, which, once started, we may hope to check only by the most effective measures to ensure rest and to conserve general health. The advantage of preventing such infections rather than trying to control them is obvious, as is the desirability of safeguarding the infant from further infection after the first seeds have been sown. However our experience coincides with that of Brailey[5] and of Rosenberg and Kereszturi,[6] who have recently pointed out that infection in infancy is not so frequently fatal as was once supposed. Also, we have observed with Brailey that when children infected in infancy die of tuberculosis, this termination usually occurs within a year after the infection is first discovered. Thus, in a follow-up study of 51 tuberculous infants discharged from the Infants' Hospital, the 25 who succumbed to tuberculosis were found to have lived less than one year after leaving the hospital. These observations, however, merely bear out the observation that the younger a child is, the more commonly a fatal outcome may be expected from direct progression of unchecked lesions.

In older children the situation appears to be characterized by a type of danger different from that which threatens the infant and young child. Although the wisdom of preventing infection and superinfection must be stressed for the older child as well as for the infant, the comparative infrequency of fatalities between six and twelve indicates that very rarely in such children is death from tuberculosis to be considered a serious and immediate threat. The pathologic process in most of those who succumb at this period of life is apparently due to the rupture of a previously unsuspected central-nervous-system focus. Such a fatal termination has at least some of the characteristics of an unpredictable accident. The management of the tuberculous child in this age period should be interpreted with this fact in mind.

In spite of efforts for prevention, a certain number of children will continue to become infected, and a very small number of them will develop central-nervous-system foci. However, one cannot diagnose the presence of such lesions in the living and apparently healthy child, except in the rare event of calcification sufficient to appear roentgenologically. Nor is there any proof that such lesions, even though their presence is proved, can be prevented from rupturing by a sanatorium regimen. Older children in whom death was brought about by this train of events did not show manifestations of impaired health before the onset of meningitis. Thus it would appear from these facts that if one believes it possible to restrain a sudden invasion of the meninges by a sanatorium regimen, he might justifiably advise such treatment for any older child who reacts to tuberculin.

In this regard it is of interest to note from Table 2 that we have not been so successful in Massachusetts in reducing the tuberculosis death rate among children as we have among infants

For infants, the 1936 mortality has been reduced to 12 per cent of the 1922 figure, while among older children a reduction only to 26 per cent of the earlier total has been obtained. One wonders if some of the difficulty in reducing mortality among these older children has not been the somewhat accidental nature of the fatal process in their age period.

According to these experiences, fatal pulmonary tuberculosis has been so rarely seen in older children as to make it of doubtful value to restrict the activity of a child because of roentgenologic findings in the chest, unless very definite parenchymal changes are present. Moreover, if clinical signs and symptoms accompany roentgenologic changes in the lungs at this age, we urge the careful consideration of a non-tuberculous as well as a tuberculous etiology.

Thus, we consider it very rarely necessary to restrict the activity of any grade-school child because of the immediate threat of tuberculosis. But if a child with unequivocal evidences of infection is allowed to lead an unrestricted life, may this render him more prone to develop tuberculosis during and after adolescence? Can the incidence of tuberculosis in the teens be reduced by extra care during childhood?

As stated above, our material does not give information except for children less than twelve years old. We can answer these questions only by quoting the opinions of men who have had wide experience. Thus, Myers, Harrington, Stewart and Wulff[7] state:

> All children reacting positively to the tuberculin test should have films made of the chest periodically, beginning at about the age of ten or twelve years. Experience has taught us that when chronic lesions of reinfection type make their appearance in the lung so as to be easily detected by the x-ray film, there is usually a long time, often two or more years, before symptoms develop. During this period most cases can be treated successfully, and many of them when adequately treated do not become open cases. We believe it is far more satisfactory in every respect to keep the potential cases under close supervision in their homes . . . than to provide treatment for the first infection type case.

Pope[8] says:

> I question whether it is possible to measure with any certainty the influence of sanatorium treatment on the development of tuberculosis in such children, on account of the large number of variables which may be concerned, and the long period for which it would be necessary to follow such children. After some thirteen years of experience in the department we feel that children with primary nodules in the parenchyma or calcified tracheobronchial lymph nodes can be safely cared for at home, if contact with open tuberculosis is broken, and the child is kept under reasonable medical supervision.

While our experience shows that a restricted life is rarely indicated for the usual type of tuberculosis in older children, this does not in the least mean that they should be dismissed from the attention of the physician without proper management of the immediate situation and a proper plan for the future. The immediate situation requires a study of the child's household for the presence of tuberculosis. The application of the tuberculin test is such a simple procedure that there is no excuse for failing to utilize it to this end. It is no longer true that all the older members of the family may be expected to be tuberculin-positive. This statement, still often made, rests upon the persistence of earlier statistics. In an interesting study[9] of the percentage of positive reactors among college students, figures have recently been published which show that by the age of about twenty only between 25 and 50 per cent of the population have been infected. There is little doubt that this percentage range will still further diminish in the near future. As a practical point, it may be suggested that when the parents object to being tested, one can usually obtain their consent to the examination of the other children. If none of the other children react, one may be less urgent about the testing of the parents. All positive reactors in the family should of course be studied by roentgenogram. By this means the immediate surroundings of the child may be freed from contact, and, as has often been stressed in the literature, unsuspected or improperly treated tuberculosis may be brought to light.

When the child's immediate surroundings have been "accredited," to use the term recently suggested by Stewart,[10] the further duty of the physician is to impress upon the parents the importance of annual roentgenological examination of the patient as he passes into and through adolescence. This should be all the more urgently advocated if the patient's roentgenogram shows scars of many or large lesions or if the family will not co-operate in the breaking of contacts. If the physician or the clinic will not only arrange such a concrete program but will also see that it is carried out, the results will be far more satisfactory than those following the dispensation of vague advice concerning rest and fresh air.

The discovery of tuberculosis in an infant should be followed by immediate and exacting measures toward conserving the patient's health and strength. Usually this means sanatorium care or its equivalent in supervision at home. After the third year of life these measures may be gradually relaxed. The discovery of tuberculosis in a schoolchild should be followed by a program directed particu-

larly toward the prevention of disease in the years of life to follow. The discovery of tuberculosis at any age calls for immediate measures to find and break dangerous contacts. The infected child always represents a clue to the potential presence of disease in the household circle. Often the investigation of the family problem represents the greatest responsibility of the physician.

SUMMARY AND CONCLUSIONS

The facts concerning a hospital series of 345 deaths from tuberculosis among infants and children have been tabulated and analyzed. The following observations seem of importance:

1. Tuberculosis mortality in infancy and childhood is rapidly decreasing.
2. Mortality is highest during the first two years of life (58 per cent of all deaths). It declines during the next five years (35 per cent of all deaths), to reach a low level in the five years from seven to twelve (7 per cent of all deaths).
3. Deaths in infancy are usually due to miliary tuberculosis, with or without an associated tuberculous meningitis. Deaths in infancy often occur in the presence of an active and advancing pulmonary tuberculosis. Abdominal tuberculosis, although rarely seen in recent years, is a much more frequent cause of death at this age than in later childhood.
4. Deaths in older children are most often due to a tuberculous meningitis not associated with miliary dissemination to the rest of the body. Such a condition was responsible for death in 75 per cent of the fatalities between the ages of seven and twelve. Fatal pulmonary tuberculosis of the adult type is extremely rare in children at this age. No death from active abdominal tuberculosis occurred among them.

The pathology of fatal tuberculosis offers certain implications as to the management of the disease in infants and children. In the light of these implications the proper care of these patients is discussed.

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INIOPAGUS

A Rare Form of Siamese Twins

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TWINS can be classified either as fraternal or as identical. The former occur almost four times as frequently, may be of different sexes, and usually resemble each other no more than children in the same family. They are also called nonidentical twins; and, being the product of development of two separate ova, fertilized at about the same time, their chorions may become adherent through crowding only. Identical or homologous twins, however, are almost indistinguishable, and are believed to be produced by the perfect division of the embryonic mass within a single fertilized ovum. They, therefore, have only a single placenta, whereas the former have two separate placentas.

Siamese twins, or double or compound monsters, are believed to be the product of an imperfectly or incompletely divided embryonic mass within a single fertilized ovum, which ordinarily divides perfectly and completely to form identical or homologous twins. This theory is stated by Bateson (quoted by Dunbar[1]) as follows: "By a division [of a single fertilized ovum], imperfectly effected, the resulting bodies instead of being complete twins or triplets may remain united together, frequently having a greater or lesser part of a body in common."

To summarize our present knowledge of the fundamental causation of monsters, gained from experimental teratology, it is fair to state that, according to Hirst,[2] faulty implantation of the ovum plus mechanical and chemical environmental influences, must be held accountable, rather than inherent germ tendencies. He cites the experiments of Stockard and other experimental embryologists, using various ova and causing twinning and double or fused monsters by retarding their development at critical periods through subjecting them to cold or reduction of the oxygen supply. That defective ova or sperms may be a causative factor is, however, neither disproved nor impossible.

These fused twins are called Siamese after the famous twins Chang and Eng, both males, joined in the midline at and just above their umbilici. They were born in Siam in 1811 and were discovered by Captain R. Hunter in 1829 when they were eighteen years old. Their mother stated that they delivered easily, the head of one being born between the legs of the other. They were examined here at Harvard in 1829 by Dr. John C. Warren and were exhibited throughout the United States and Europe, but were barred from France because of their possible effect on pregnant women. They finally settled in North Carolina as farmers, under the name of Bunker, and married. Chang had six children; Eng had five. They died in 1874, Chang being found dead in bed one morning, and Eng dying a few hours later. Postmortem examination showed a communication between their portal systems, with a thin bar of liver tissue extending through the connecting band. Curiously enough, Chang was intemperate, but his potations had no effect on his brother. Teratologically they constituted a common type of twins, called xiphopagus, a species of thoracopagus. Many reports of such twins appear in the literature.

Briefly, equal or symmetrical double monsters, or diplopagi, are always identical twins and may be classified as follows:

I. *Teras anadidymum* — twins divided at their cephalic poles only. These monsters vary from those with double faces to those with double heads, usually without division of the neck, and are joined at the sides and the backs of the heads. Occasionally there are two heads, necks and chests, joined laterally on one lower trunk and pelvis, as in the case of the Tocchi boys, born in 1877 and reported by Harris[3] as living at the age of sixteen.

II. *Teras catadidymum* — twins divided at their caudal poles only. These monsters include:

1. Dipygus — a fused monster with double legs, with or without a double pelvis (not strictly a symmetrical monster).

2. Craniopagus — twins united at the heads only. Such cases are rarely joined by brain tissue. This subgroup includes:

a. Craniopagus parietalis — twins joined by parietal bones, said to be the commonest. Ahlfeld[4] collected 12 cases from the literature.

b. Craniopagus occipitalis or iniopagus[5] — twins joined by the occipital bones or inion. This is the rarest type. Ahlfeld[4] was able to collect but 5 cases, only 1 of which survived for an appreciable period.

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c. Metopagus — twins joined by the frontal region. Only 3 cases have survived for any period — 1 for ten years (case of Sebastian Munster,[6] 1495).

d. Acrocephalus pagus or cephalopagus — twins joined by the tops of the heads. Hirst[2] cites 6 cases.

III. *Teras anacatadidymum* — fused twins divided approximately at both poles, with more or less fusion of the thorax, abdomen and pelvis. These monsters include:

1. Thoracopagus — twins joined only in the thoracic and upper mid-abdominal regions. They form the largest group. Those joined only in the regions of the umbilicus and up to the xiphoid cartilage are classified as xiphopagus, of which the Siamese twins are an example. Two other famous examples are the Hindu sisters, described by Berry[7] in 1821, and the Orissa sisters,[8] born in India in 1887. In 1902 Baudouin[9] reported 16 thoracopagi born living. In the tenth century there were reports of 2 cases, 1 was doubtful, but the other, an Arabian case, was very likely authentic. A third thoracopagus, born in 1429 at Aubervilliers, France, was said to have lived a few days, and was visited by more than a million Parisians. Since then many other cases have been reported. In 1933, Ho[10] delivered a thoracopagus, with both twins dead, weighing 8½ lb. The first twin was delivered by forceps, the second by version. In 1936, Courtright and Austin,[11] after an attempted breech extraction for a prolapsed cord, had to resort to a cesarean section, and found a 14½-lb. thoracopagus, dead, the mother dying of septicemia on the fifth day. Another case of considerable local interest was that encountered by Dr. Clarence H. Staples,[12] of Malden, who on December 5, 1932, delivered a 9½-lb. thoracopagus that showed fusion of the hearts and livers, along with a normal 6-lb. triplet, who is still alive and well. According to Hirst[2] the incidence of craniopagi as compared with thoracopagi is 1:43.

2. Pygopagus — twins joined by the posterolateral aspects of their sacrums. They are very rare, but eleven times commoner than craniopagi. The Gibbs sisters of Holyoke, Massachusetts, are a recent example. The twins are usually females and may have fusion of ani, genitalia and even spinal cords.

3. Ischiopagus — twins joined by fusion of the pelves, end to end. Cooper's[13] case is an example. These twins had four legs, two on each side of the line of fusion and at right angles to their bodies. They were both females. Curiously enough, however, the genitalia and ani were placed on the right side of each child, between its right leg and the left leg of the other. They had only one umbilical cord. This is a rare type, but four times commoner than craniopagi.[2]

4. Ectopagus — twins connected along the sides of their bodies. The inner arms or legs are represented by a median limb.

Unequal or unsymmetrical double monsters consist of a normal or nearly normal autosite and a quite incomplete parasite attached to the first. One type is a parasite consisting of a head with or without arms, or of legs, or of the lower trunk with legs, usually attached at or near the epigastrium of the autosite. An example, cited by Hirst,[2] was Colloredo, born in Genoa in 1617, the parasite consisting of a trunk, two arms and a well-formed head. The eyes remained closed and the monster took no nourishment. Other examples are the Hindu, Laloo, and the Chinese boy, A-Ke.[2] Another type has a head or a part of a head attached to the head of an otherwise normal individual, such as a two-headed Janus. Under this category is a janiceps, a monster having two heads fused together, the faces, one of which may be very small, looking in opposite directions.

Because of the extreme rarity of fused monsters, no statistics are available as to their incidence. In fact, such cases are so uncommon that statistics from hospitals or clinics even over periods of twenty or thirty years are of little value. Adair,[14] in a report of 25,000 pregnancies at the Chicago Lying-In Hospital, found 2 double monsters. Hirst,[2] in a series of 20,170 births at the University of Pennsylvania Hospital, found only 1 double monster, a dicephalus. In all recorded literature only 5 other cases of iniopagus can be found,[15] indicating that the frequency of this monstrosity must be one in many billion births. Curiously enough, another example,[16] apparently an iniopagus, was born in Michigan City, Indiana, a month after the delivery of the following case.

CASE REPORT

Mrs. M. F., aged 24, in her third pregnancy, had a moderately difficult first delivery with low forceps. The second delivery, 2 years before the present pregnancy, was an easy, almost spontaneous breech delivery performed at home under ether analgesia. I first saw the patient on April 15, 1936. She was due for delivery on June 22. She was in excellent condition: there was no edema and the urine was negative. The heart and lungs were normal. The blood pressure was 120/80. The pelvic measurements were I. C. 31 cm., I. S. 26 cm., E. C. 20 cm. The pelvis was normal. There seemed to be a large amount of amniotic fluid.

On June 3 I saw the patient again. She had a vertex presentation with a floating head, the urine was negative for albumin, and the blood pressure was 120/80.

On July 1 I saw the patient at her home at 10.30 a. m.

in active labor. She seemed to be carrying a large baby with a floating head. A prominence which I took to be the forehead of the flexed head appeared to be on the mother's left. The fetal heart beat was 140 in the right lower quadrant of the abdomen. Twins were not even suspected. Rectal examination showed the head to be high, the cervix 1½ fingers dilated, and the membranes intact. Again, there seemed to be an excess of amniotic fluid.

At 2.30 p. m. the patient was fully dilated, as determined by rectal examination, so a vaginal examination was made to check the dilatation and to find out if the head would engage. Pressure on the fundus made the head come into the pelvis to the ischial spines, and since the cervix was fully dilated the bladder was catheterized and the membranes ruptured. The patient was having strong 40- to 50-second pains every 1½ or 2 minutes and bearing down with each pain. At this point it was thought that the delay in engagement was due to a large baby whose head needed further molding. Judging by the sutures the presentation was LOA, which was confirmed by palpation of the baby's face in the right posterior position. However, it was noticed that the sagittal suture was not in the midline heading directly down through the pelvic canal, but seemed to be headed slightly toward the mother's right leg.

At 3.30 p. m. the head was at the level of the spines, and had been there with the cervix fully dilated for about 1 hour without progress. It was therefore decided to deliver the patient by forceps. At 3.45 the patient was under anesthesia, and a forceps was applied for an LOA position. Much to my surprise, no application could be made; the ends of the blades seemed to be kept apart and open, so that no purchase could be obtained. Palpation of the face checked the position as correct, but showed that the head was very long.

At about 4.30 p. m. I decided to do an internal podalic version. The head was pushed up into the left iliac fossa and then, inserting my left hand into the uterine cavity, I discovered twins. I brought down the two feet of the baby which had been presenting by the vertex, and, completing the version, began to extract the infant fairly easily until just before the shoulders were to be delivered. The back persisted in facing the mother's right thigh, and palpation in the vagina showed that the baby's face was in a transverse position, facing the mother's left and slightly anterior. The baby moved and breathed, but the cord finally stopped pulsating. The mother's condition was excellent. After persistent effort to rotate the chin posteriorly from the left anterior to the left posterior position so as to make the occiput anterior, the chin was finally rotated into the left posterior position. This was accomplished by direct force, applied inside the vagina by grasping the chin and face with the right hand, and crooking the right index and middle fingers inside the baby's mouth against the hard palate.

This rotation having been accomplished, the head could not be rotated the remaining 45 degrees to make the occiput anterior, and the shoulders could not be delivered. Since the head seemed very long, I decided upon decapitation and craniotomy. Fortunately, however, I could not reach the neck to cut it, so that procedure was given up. With added traction and suprafundal pressure, the head was finally started, and after the slow emergence of what seemed an extremely long head I saw another face on the other side; following what was really a second head came the conjoined smaller twin.

There was only a 2-cm., first-degree tear. There were two cords, which met on one placenta so that their vessels anastomosed freely. Together, the babies, both females, whose bodies are preserved in the Warren Museum, weighed 13½ lb. The larger one weighed about 8½ lb. They were perfectly formed and developed, and

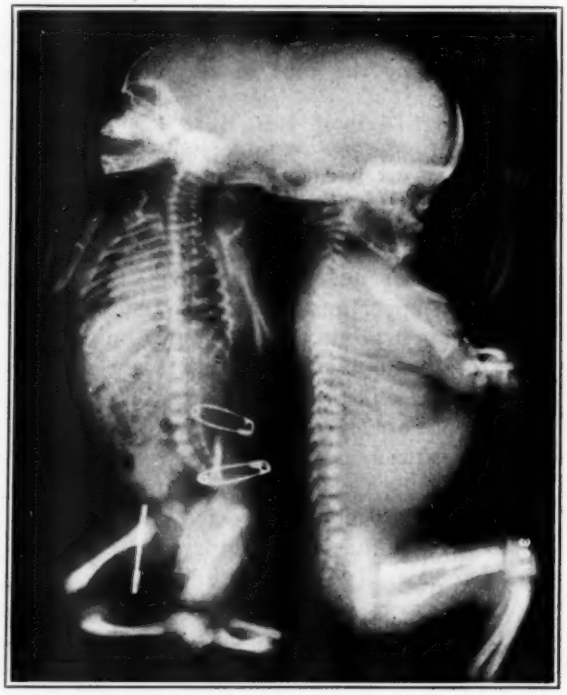

Figure 1. *X-ray photograph of twins, showing focal union of heads. In the larger baby picture note the fracture of the right humerus at junction of the upper and middle thirds. This fracture was an accident of delivery. Note also the non-aeration of the lungs of the larger dead baby and the contrast in the aerated lungs of the smaller living baby.*

attached to each other by the occiputs only. The larger one took several breaths and the smaller one began to cry lustily just after I had told the family it was a blessing that they were dead.

Figure 2. *Iniopagus twins, side view, showing the attached heads.*

The mother had an uneventful convalescence. The smaller twin took nourishment after being removed to the Lawrence Memorial Hospital in Medford but later failed, and died 38 hours and 50 minutes after its birth. Death was undoubtedly due to toxic absorption from the dead

sister. Any attempt at separation by surgery was obviously impossible, as is evident from the photographs and x-rays.

The diagnosis of double monsters before delivery is theoretically possible if all cases in which twins are suspected are x-rayed. DeLee[17] states that the condition has never been diagnosed before delivery. Usually the diagnosis is made after

Figure 3. *Iniopagus twins, back view, showing the somewhat eccentric attachment of the heads.*

delivery, or during it because of dystocia. In general, breech extraction of one or both of the twins is the best method of delivery if it can be effected from below. If the diagnosis is made in advance of delivery, one might conceivably consider cesarean section, especially if the double mass appears to be large. Naturally no consideration should be

Figure 4. *Iniopagus twins, top view, showing ridge of union and separation of hair.*

given the monster, especially if the mother's life is endangered. DeLee states that experience has shown that it is better to deliver the whole mass and not to amputate the delivered portion. Cesarean section after attempted vaginal delivery is dangerous and should not be done except as a last resort.

SUMMARY

The various types of double or compound monsters are discussed and a case report is given of a very rare type — iniopagus.

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Discussion

Dr. Arthur T. Hertig,* Boston: Dr. Vernaglia's excellent paper has left little to discuss so far as the etiology of abnormal twinning is concerned, since the more we try to explain it the more we are forced to reiterate that apparently a phase has persisted which should ordinarily occupy a very short time in the life of an ovum in the act of twinning normally.

It may be interesting for you to learn of some of the theories as to the formation of monsters in general — since these symmetrical, conjoined twins are really monsters. However, since they are obviously twins as well, we shall have to discuss twinning in addition to monster formation.

The accepted belief for a long time was that monsters were, in general, freaks of nature; in other words, Nature was amusing herself. A second belief which held sway for some time was that monsters were an attempt on the part of supernatural forces to warn mankind against impending calamities; indeed, the Latin verbs, "to warn" and "to indicate" are *monere* and *monstrare,* which indicates the origin of the term "monster." As long ago as 2000 B.C. there were cuneiform inscriptions depicting many of the same sorts of monsters which we see at the present time, together with some of the impending disasters against which they were supposed to warn.

Still another theory was that monsters were the result of intercourse during menstruation. One has such an example in the mythical god Vulcan. We also see evidence of this belief in certain religious teachings even at the present time, namely the Hebrew warning that menstruous women who conceive shall bring forth monsters. Another notion was that sexual intercourse between man and the lower animals would result in monsters, for example the Centaur.

Later on, prenatal influences were mentioned as a cause, and we see all sorts of evidence of this belief in religious writings, such as *Genesis,* and in plays, such as *The Merchant of Venice.*

More recently, mechanical factors such as blows and falls have been thought to play a role in the genesis of monsters, but this theory is now largely discredited. Such is also the case with monsters with amputated digits supposed to be due to the formation of intrauterine adhesions. It has lately been shown by Dr. G. L. Streeter that these adhesions are a result rather than a cause of certain congenital abnormalities. In adults, moreover, there is a disease called ainhum in which the digits drop off with

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increasing age. This is analogous to the spontaneous intrauterine amputation of digits due to a congenital anomaly of the affected parts.

We now come to the modern theories, which have been so adequately discussed in this paper. They emphasize the altered physical or chemical factors demonstrated by the classic work of Stockard. He showed that lowering of the temperature or of the oxygen tension could result in any number of abnormalities, including various sorts of twins. Many different procedures resulted in the same abnormality. Therefore, the time at which a given noxious stimulus was applied to the ovum, rather than the way in which the environment was altered, determined the resulting congenital anomaly. This investigation led to speculation regarding human monsters, as to whether toxic products of disease, alcoholism, lead poisoning, phosphorus poisoning, and so forth, could or did result in monsters. It has been demonstrated through the classic researches of Evans and Bishop in 1923 that vitamin E deficiency, at least in the case of the white rat, results in the death of the fetus, with resorption of the placental site.

As for the application of Stockard's work in twinning, his theory can be adapted in this way: if the embryonic axis, which determines the way the embryo shall form, loses its dominance because of the altered physical environment of the ovum, other embryonic axes form and the resulting embryos become the twins or the triplets of that ovum.

There are three types of twin formation, normal as well as pathologic.

The first is the splitting of the inner cell mass of the ovum, which is potentially embryonic, into two, four or even six different parts. Six has been given as the maximum number of possible offspring in a human pregnancy. This type of twinning obviously has to take place before the amnions are formed, and will result in two complete embryos, each in its own amnion but both within a single chorion, in other words, identical detached twins having a single placenta. This is the type of twinning that has a hereditary basis and tends to run in families. It is about four times as common in such families as the sporadic type of twinning, which is embryologically a pathologic phenomenon.

In the second type of twinning, the germ-disk area has two or more potential points for embryonic formation, but without separation of the germ disk into the corresponding number of parts. This represents the type of twins in which there is a single amnion — in the case of human twins — containing two or more embryos with distinct cords.

The third type concerns a single embryonic axis on the germ disk, splitting either partially or completely. Authors who say that the germ disk splits entirely maintain that these conjoined monsters or conjoined twins are the result of the subsequent re-fusing of the two embryonic axes. On the other hand, there are those who insist that the embryonic axes have never completely separated in the first place.

The proof of the correctness of these various theories therefore awaits further study of more material.

THE USE OF PROSTIGMIN AS A PREPARATION FOR ABDOMINAL ROENTGENOGRAPHY

A Preliminary Report

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FROM earliest times in the application of roentgenology, flatus involving the intestinal tract has been a disconcerting factor in the study of organs in the abdominal cavity. Various agents have been employed in an attempt to rid the cavity of gas. Most of these, including enemas of various kinds, have caused discomfort to the patient and have been unreliable so far as effectiveness is concerned. The object of this communication is to report a series of cases in which Prostigmin was administered for this purpose.

The physiological features of eserine, an alkaloid of physostigma, have long influenced its use as an agent to combat postoperative distention. Its employment, however, is necessarily restricted because of the frequent unpleasant side effects — slowing of the heart due to vagus stimulation, rise in blood pressure, respiratory depression, dyspnea and miosis. Chemically, eserine is of interest as an example of an alkaloid the physiologic action of which is dependent on the presence in the molecule of a particular radical, in this case the methylcarbamic-ester radical. The studies of Stedman[1] and his co-workers[2] show that compounds possessing miotic activity are basically substituted phenyl esters of monoalkylcarbamic acids. They found that activity was greatest with a methyl radical, that is, one similar to eserine, while no activity was observed when the radical was a phenyl.

Subsequently Aeschlimann and Reinert[3] made a comparative study of a series of some forty alkyl, aryl, dialkyl and arylalkyl carbamic esters of phenols containing a basic substituent directly or indirectly attached to the phenyl radical. It was found that the dimethyl carbamic ester of 3-hydroxyphenyl-trimethylammonium methylsulfate possessed the most desirable pharmacologic and chemical features, as compared with eserine, of any of the compounds studied. The substance

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has been marketed under the trade name of Prostigmin. Chemically, in relation to eserine, the new drug has a less complicated structure and possesses greater stability. Pharmacological studies show that Prostigmin has a more marked action on peristalsis than has eserine, a less pronounced miotic effect, and is almost completely devoid of cardiac side effects.

Aeschlimann and Reinert found, in the frog, that eserine in a concentration of 1:1000 often stopped the isolated heart in diastole, whereas in identical concentration Prostigmin at most caused a slight decrease in amplitude. A 1:100 concentration of eserine almost invariably stopped the heart in diastole, but a corresponding concentration of Prostigmin usually caused only a decrease in amplitude. With the isolated rabbit intestine Prostigmin is still active in dilutions of 1:5,000,000; in some cases a definite increase in tonicity was found even in dilutions of 1:7,500,000. Berk[4] observed that the isolated frog heart subjected to the action of strophanthin was stopped in diastole following treatment for from five to seven minutes with a 1:2000 solution of eserine salicylate. Under similar conditions, Prostigmin solutions of varying concentrations (1:5000 to 1:8000) were without influence, and the heart was stopped in systole.

Rothschild[5] compared the peristaltic action of Prostigmin with that of other parasympatheticomimetic substances on the normal, isolated small intestine of the guinea pig. He found that Prostigmin had a decidedly stronger peristaltic action than had eserine on the intestine rendered atonic either by atropin or adrenalin. It restored tonicity to a greater than normal degree. Under the influence of papaverine the tonus of the intestine slowly decreased. Treatment with Prostigmin checked this decrease and gradually stimulated the intestine almost to the normal point. Under similar conditions, eserine caused great variations of tonus but did not restore normal peristaltic conditions, the tonicity remaining below its initial level.

The clinical literature on Prostigmin is quite extensive. References for the most part concern the effectiveness of the drug in the field of surgery to prevent postoperative distention and restore intestinal motility, and in medicine as a treatment for myasthenia gravis. The expanding literature is indicative of the increasing use of the drug in these fields. Papers by Levis and Axelman,[6] by Hendler[7] and by Uznanski[8] are representative of recent contributions to the literature on the use of Prostigmin in surgery. Levis and Axelman treated some 88 cases, in which the use of the drug was attended by a highly satisfactory clinical response. They concluded that Prostigmin has proved the most effective preventive of postoperative intestinal atony, and that its use was not followed by untoward effects or systemic or local reactions, nor was the blood pressure or cardiac action interrupted. Hendler had 249 cases in his series, the drug being used prophylactically. The author stresses the satisfactory clinical response and the absence of miotic and cardiac side effects. Uznanski's report concerns the use of the drug operatively and postoperatively in both gynecologic and obstetric cases.

Saegesser[9] reported that even in cases of diffuse peritonitis no changes in the blood pressure or pulse rate due to the drug were observed. Schwerk[10] has not observed any ill effects on the heart or central nervous system. Carmichael, Fraser, McKelvey and Wilkie[11] in studying normal subjects found that Prostigmin by injection produced active movements in the colon, as evidenced by contractions and relaxations. The drug was of value in cases of gaseous distention, although an enema was necessary in order to get a satisfactory passage of flatus. These authors also found the drug free from side action on the heart rate and blood pressure when given in doses at least double those recommended.

The effectiveness of Prostigmin as an agent in the treatment of myasthenia gravis was discovered by Walker,[12] of London. Other authors[13, 14] have confirmed her observations, and in this country an increasing number report the prompt clinical response to the drug and its value both in the diagnosis and treatment of this condition. Everts,[15] of the New York Neurological Institute, first called attention to the oral use of Prostigmin in myasthenia. Other contributions include the papers of Winkelman and Moore,[16] Viets and Mitchell,[17] Riven and Mason[18] and Thorner and Yaskin.[19]

While the known pharmacology of Prostigmin suggests its usefulness in roentgenology, a thorough search of the literature discloses no case in which the drug was used for dispelling gas shadows prior to x-ray examination. Other preparations, however, have been employed. Ritvo[20] concluded that Mecholyl and physostigmine were valuable aids in studies of the gastrointestinal tract. He pointed out that physostigmine should not be used in cases of late pregnancy, severe heart disease or iritis. Pitressin has been found by Collins and Root[21] to be valuable in the elimination of confusing gas shadows during cholecystography and has been used to eliminate intestinal gases by others.[22–25]

A total of 37 cases are included in our preliminary study. With but few exceptions, the subjects were regularly committed patients of the Metropolitan State Hospital. Each patient received 2 cc., the deliverable contents of two ampules, of Prostig-

min (1:2000) the night before the examination and an identical dose the following morning, one hour before the examination. No other procedures or special diet formed part of the preparation. In every instance the patient experienced increased intestinal action twenty to thirty minutes after the drug had been administered. There were no complaints of abdominal distress, and no change in cardiac action could be detected, although in a few cases the patient had a known cardiac lesion. No visual disturbances were reported, and at no time did the drug have an undesirable effect on the mental condition. The results are summarized in Table 1.

Table 1. *Summary of Results.*

Case No.	Kind of X-Ray Photograph	Result
1	Pyelogram	Good
2	Pyelogram	Good
3	Pyelogram	Excellent
4	Pyelogram	Good
5	Cholecystogram	Good
6	Cholecystogram	Good
7	Cholecystogram	Good
8	Cholecystogram	Good
9	Cholecystogram	Good
10	Intravenous cholecystogram	Good
11	Flat plate of abdomen	Good
12	Flat plate of abdomen	Good
13	Flat plate of abdomen	Good
14	Flat plate of abdomen	Good
15	Flat plate of abdomen	Poor
16	Flat plate of abdomen	Excellent
17	Flat plate of abdomen	Excellent
18	Cholecystogram	Good
19	Flat plate of abdomen	Excellent
20	Flat plate of abdomen	Good
21	Flat plate of abdomen	Excellent
22	Intravenous pyelogram	Excellent
23	Plate of lumbosacral spine	Good
24	Intravenous pyelogram	Good
25	Intravenous pyelogram	Excellent
26	Cholecystogram	Excellent
27	Intravenous pyelogram	Good
28	Intravenous pyelogram	Good
29	Flat plate of abdomen	Excellent
30	Flat plate of abdomen	Excellent
31	Cholecystogram	Poor
32	Intravenous pyelogram	Excellent
33	Intravenous pyelogram	Good
34	Intravenous pyelogram	Excellent
35	Cholecystogram	Good
36	Plate of lumbar spine	Good
37	Flat plate of abdomen	Excellent

Excellent: no flatus, or only a very slight amount.
Good: a small amount of flatus, but not interfering with visibility.
Poor: any amount of flatus interfering with visibility.

SUMMARY

The pharmacologic features of Prostigmin, the dimethyl carbamic ester of 3-hydroxyphenyltrimethylammonium methylsulfate, is indicative of its usefulness in roentgenology.

This communication concerns its use as an agent to dispel gas in preparation for x-ray studies of conditions related to the abdominal cavity.

The results show the drug to be very useful for this purpose.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 24341

PRESENTATION OF CASE

A twelve-year-old, white, American schoolgirl entered the hospital with the complaint of fever of six weeks' duration.

She had been perfectly well until six weeks before entry, when she quite suddenly had a chill and developed a temperature of 104°F. She had had no preceding upper respiratory infection or other symptoms except for transient pain in her left wrist and elbow which lasted one day. Her urine was cloudy at that time, and her physician said there were white cells in it. She was given Prontylin in a dosage of five tablets per day for a few days and improved somewhat. Her temperature, however, continued to range between 99 in the morning and 103 or 104°F. in the evening. She was studied for a period of a week in a hospital: it was reported that there were red cells and white cells in her urine. Three weeks before entry she had a swollen tender area on the right side of her neck, which cleared up in one day. About that time she was given pyridium and mandelic acid for short periods without much if any improvement. Five days before entry she had a dull, almost constant frontal headache lasting two days. During her illness she had moderate nosebleeds almost daily from the right nostril, but no bleeding elsewhere. For the three years before entry she had had occasional nosebleeds. Her appetite was fair, and she took fluids well. She had no hematuria or other genitourinary symptoms and no cardiorespiratory or gastrointestinal symptoms. She was thought to have lost about 10 lb. during her illness, but aside from that and the epistaxis her only persisting symptom was the remittent fever. About seven years before entry she had had an unexplained fever for a brief period, and was carefully studied, but no definite diagnosis was made. She had no joint pains, chorea or anything else suggestive of rheumatic fever at that time. Her older sister, however, had had a definite attack of rheumatic fever. Her father had had arrested tuberculosis for twenty years. His last x-ray had been taken about nine years before his daughter's illness. He had no symptoms except a persistent cough which he attributed to a winter cold. The patient's past history and family history were otherwise negative. Her growth and development had always been normal.

Physical examination revealed a pale, thin girl in no acute discomfort. There were questionable petechiae on the hard palate, and nontender glandular swelling could be palpated at the angle of the right mandible. The lungs were negative except for coarse rhonchi which could be heard over the right scapula. There was questionable slight enlargement of the heart to the left, and a soft systolic murmur could be heard over the apex. The blood pressure was 102 systolic, 80 diastolic. The abdomen was negative, but on deep palpation there was bilateral costovertebral tenderness. There was no pain or limitation of motion of the joints.

The temperature was 101°F., the pulse 90. The respirations were 22.

Repeated urine examinations showed a specific gravity varying between 1.004 and 1.020. A urine concentration test showed a maximum specific gravity of 1.021. The urine always contained albumin, varying in amount from the slightest possible trace to a trace. It never contained sugar, acetone or bile. The sediment occasionally showed a few red cells, consistently showed moderate numbers of white cells, often in clumps, and usually showed a few to many hyaline, granular and cellular casts. The blood showed an admission red-cell count of 3,000,000 with 55 per cent hemoglobin, which gradually fell in spite of treatment to a terminal level of about 2,000,000 with 40 per cent hemoglobin. The admission white-cell count was 4800 with 79 per cent polymorphonuclears, 15 per cent lymphocytes, 4 per cent monocytes and 2 per cent eosinophils. There were 8 per cent reticulocytes. The white count remained fairly constant between 5000 and 8000, but on several occasions rose as high as 12,000. The differential remained essentially the same as on admission. The guaiac test on the stools was negative. The blood Hinton test was doubtful once and positive once; the blood Wassermann, weakly positive twice. Three blood cultures gave no growth, and two stool cultures were negative for pathogenic organisms. Agglutination tests for typhoid, paratyphoid and undulant fever were negative. A 1:100 tuberculin test was twice negative. A culture of a catheterized urine specimen showed *Bacillus coli*. The corrected sedimentation rate was 2.1 mm. per minute. The fasting blood sugar was 113 mg., the nonprotein nitrogen 31 mg. and the total cholesterol 165 mg. per cent. An electrocardiogram was normal.

X-rays of the chest showed no cardiac enlargement or pulmonary lesions. A flat film of the abdomen was negative, and an intravenous pyelo-

gram showed prompt excretion of the dye on both sides, with normal kidney pelves and ureters. The spleen appeared to be slightly enlarged.

During her two months' stay in the hospital she ran a practically continuous remittent fever, the daily peak varying from 99 to 104°F. Her pulse ranged between 90 and 120. During the first three weeks the costovertebral tenderness increased somewhat and was a little more marked on the left. She also complained of slight pain in that region. At the end of that time *Bacillus coli* was again cultured from the urine. Repeat x-rays of the chest two weeks and four weeks after entry were negative. The costovertebral tenderness had entirely disappeared by the end of the first month, but her general condition was so poor that it was necessary to give her a blood transfusion. Except for some emaciation the physical examination was essentially negative at that time. One observer thought there was slight edema of the face and questionable shifting dullness in the flanks. The blood pressure was 105 systolic, 50 diastolic. An x-ray of the chest showed diminished radiance in the right midlung field, which was thought possibly due to early consolidation. The serum protein was 4.7 gm. and the nonprotein nitrogen 48 mg. per cent. Four days later there was definite, marked enlargement of the heart. The sounds were loud, there was a gallop rhythm, and the systolic murmur was easily audible at the apex. There was also some widening of the intercostal spaces on the left, with dullness and rales in the left lower lobe posteriorly. The face and hands were somewhat puffy, but there was no venous engorgement and the abdomen was still negative.

A portable x-ray of the chest taken three days later, on the thirty-eighth hospital day, showed increase in size of the heart shadow both to right and left. The left diaphragm was not visible because of hazy dullness at the left base. An electrocardiogram showed a shift of the axis with inversion of T_2, T_3 and T_4 and decreased QRS voltage. The P-R interval was normal. An x-ray of the chest taken on the forty-fifth day showed further increase in the size of the heart shadow and increase in the amount of fluid in the left pleural cavity. On the following day an attempt was made to do a pericardial paracentesis at a point below the left nipple and 1 cm. to the left of it. About 15 cc. of straw-colored fluid was removed which contained 7350 white cells with 40 per cent polymorphonuclears and 60 per cent lymphocytes, but no red cells. After removal of the fluid 15 cc. of air was injected through the needle. The following day an x-ray of the chest showed no decrease in the size of the heart shadow and no air visible in the pericardium. However, there was a small amount of air in the left pleural cavity.

An electrocardiogram on the fifty-first day showed slight right-axis deviation and upright instead of inverted T waves. On the fifty-fourth day it was noticed that she had developed some erythematous macular lesions on the face and around the eyes. There were also macules, which had a violaceous color, on the extensor surfaces of both arms and at the bases of both thumbs. Two days later she had a sudden shaking chill lasting about an hour. Her temperature rose to 105°F., and she complained of difficulty in breathing. The heart sounds were loud and forceful, and coarse rhonchi were heard at both lung bases. There were also rales at the right base and some bronchial breathing in the left axilla. Her blood pressure was 100 systolic, 40 diastolic. The following night she had eighteen convulsions which lasted about two minutes and were characterized by tonic and clonic movements, deviation of the eyes upward and to the right, fixation of the pupils, and incontinence. The convulsions could not be controlled by Luminal. She became irrational, with occasional lucid intervals. She died the next day, her fifty-seventh hospital day.

Differential Diagnosis

Dr. Lewis W. Hill:* This is a long and complicated history. It might be well to boil it down before proceeding to discuss it.

This girl died of an acute infection of fourteen weeks' duration, which had a sudden onset, high temperature from the beginning, and pus and colon bacilli in the urine. She had costovertebral tenderness for three weeks. In the beginning the kidney function was not greatly impaired, as shown by a normal nonprotein nitrogen. Later this was somewhat elevated. There was no obstructive lesion of the genitourinary tract. The white count was continually low. The differential showed a polymorphonuclear leukocytosis. There was marked anemia. The blood cultures showed no growth. The heart was apparently normal at the time of entrance and four weeks later. Eleven weeks after her illness she began to have symptoms of cardiac disturbance and evidence of infection of the left pleural cavity; three days before death, a macular eruption; and the day before death, convulsions.

It seems to me that this girl's illness might well be divided into two phases, one lasting eleven weeks and one lasting three weeks. In the first phase she had no cardiac symptoms. In the sec-

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ond phase she did have cardiac symptoms. When this girl entered the hospital she presented the problem of a long-continued, obscure, high temperature of the remittent type without very much to show for it on physical examination. In this part of the country typhoid fever, tuberculosis, undulant fever and possibly ulcerative endocarditis come into one's mind in differential diagnosis.

There is nothing about the child to make one believe that she had tuberculosis, in spite of the fact that the father had had it at one time. Furthermore, the tuberculin test in dilutions as low as 1:100 was negative twice. So I think we can discard tuberculosis as a possibility.

If she had had typhoid fever she should have been getting better at the end of six weeks instead of worse. She had two negative Widal tests, so we can discard typhoid fever.

Undulant fever might be a possibility, but as a general thing in undulant fever, in spite of the fact that the temperature is high, the infection is not likely to take hold of the patient as hard as this disease did. The white count is consistent with the diagnosis, but the differential is not, because in undulant fever although the white count is low there is usually a mononuclear formula sometimes going as high as 80 per cent. Then she had two negative agglutination tests for undulant fever; so we can rule that out.

Then we come to the question of ulcerative or malignant endocarditis. It is uncommon in children but certainly ought to be considered. It usually comes, as you know, on top of an old rheumatic fever or congenital heart disease. This child, so far as we know, had had no rheumatic fever and had no congenital heart lesion. Furthermore, at the time of entrance the heart was not enlarged, and all it showed was a slight systolic murmur which I should take to be functional or a hemic murmur. There is nothing about the examination of the heart when she entered to suggest that there was any disease therein. Furthermore, after she had been in a month the record says the physical examination was essentially negative. That means no heart murmurs were heard, and there was no enlargement of the heart. So I think we can rule out ulcerative endocarditis. We then come to the question of pus in the urine. This was a disease of violent onset, characterized by high fever from the very beginning and starting with a chill, and from the start she had a certain amount of pus in the urine, with colon bacilli consistently present. With these urinary findings one expects that she had some trouble in the kidney, and if one also takes into consideration the costovertebral tenderness which lasted for three weeks, one can be reasonably sure of it. Costovertebral tenderness is quite a reliable physical sign, and I think it almost always means some infection in or about the kidneys. The only thing against kidney infection is the low white count, but a low white count sometimes accompanies kidney infection just as it occasionally does pneumonia. So it seems to me that this child at entrance to the hospital had infection in or about the kidneys. When I say "in the kidney" I mean small foci of infection in the cortical substance, and when I say "about the kidney" I mean perinephritis. In this particular situation the most likely possibility is small foci of infection, possibly with abscess formation, in the cortices of both kidneys. That she did not have an obstructive lesion of the genitourinary tract was shown by the normal pyelogram, and she certainly did not have the ordinary garden variety of pyelitis consisting of infection of the pelvis of the kidney. Her trouble was more likely in the kidney itself. I do not suppose that this child's positive Hinton and Wassermann tests had anything to do with her present disease, the marked anemia was probably due to the nosebleeds she had had and the fact that she had been sick with sepsis for six or eight weeks.

The second phase of this patient's illness is difficult to explain. She went along in the hospital for about eleven weeks about the same, not doing very much one way or another. Then she began to get worse. It was noted that her heart was very distinctly enlarged both by physical examination and by x-ray and also that she had certain signs of fluid or possibly consolidation in the left chest. The only three things that can enlarge the heart are hypertrophy, dilatation or liquid in the pericardial cavity. This child certainly could not have had enlarged heart from hypertrophy because hypertrophy does not happen so quickly. This was a quick enlargement; therefore, it was due either to dilatation or to fluid in the pericardial cavity. The differential diagnosis between dilatation of the heart and fluid in the pericardial cavity is not an easy one to make. Even with x-rays it may be difficult. As you can see from the x-rays she had a very wide heart. It was out to the right but not very far out. I think it is hard to tell how much of this shadow on the left is due to the heart and how much to fluid in the pleural cavity. If she had fluid in the pericardium it would have likely been a purulent fluid and she must have had a large amount of fluid with that x-ray picture. If she had a large amount of fluid in the pericardium her heart sounds would not have been so loud as they were. Furthermore, she lived for about fifteen days after this heart episode took place. It does not seem likely to me that if she had had a purulent pericarditis she would have

lived so long. The fluid in purulent pericarditis accumulates very quickly and may reach a large amount in a few days, and it seems most likely that if she had had purulent fluid in the pericardium it would have accumulated more quickly and killed her before that. As to the pericardial tap, the lung overlaps the heart on the left side, and therefore, particularly if there is any question of pleural involvement, one may not get into the pericardial cavity at all from a tap on that side unless one uses a long needle and goes in quite far, and even so one is going to penetrate the lung and pleura. I should imagine that the pericardium had not been entered. I do not believe we can be sure of that, but it seems likely that what was tapped was the pleural cavity. I admit that we cannot be sure about ruling out purulent pericarditis; it does not seem very likely, however, in spite of the x-ray.

Then we are left with the question of dilatation. This child had a gallop rhythm. That is in favor of myocardial trouble and dilatation. The heart evidently quieted down after a little while, and the gallop rhythm disappeared. I cannot interpret the electrocardiogram. I should think it was likely, but I would not be too sure of it, that this child had a considerable amount of fluid in the left pleural cavity and had dilatation of the heart with myocardial trouble from her long-continued septic condition. Why did fluid accumulate in the pleural cavity? It may have been by hematogenous distribution or by direct extension from the left kidney. The left kidney is higher than the right and lies quite close to the diaphragm. I think it is quite possible that she may have had a cortical abscess of the left kidney, which ruptured. What organisms might be involved? We know she had colon bacilli in the urine. That the colon bacillus was the entire cause seems very doubtful. I should think a streptococcus was working somewhere in spite of the fact that it was not recovered from the urine culture.

I should say as a diagnosis that this child probably had multiple abscesses of both kidneys and a perinephritic abscess on top of the left kidney, with fluid in the pleural cavity, probably purulent in nature, that she had septicemia and that some organism, probably the streptococcus, was recovered from the blood, that she had a terminal pneumonia and that she had a dilated heart and myocarditis. I suppose that this skin eruption that she had toward the end was the terminal eruption of sepsis and that the convulsions were terminal, although it is possible that she had an agonal meningitis.

Clinical Discussion

Dr. Harold L. Higgins: The Children's Medical Service tended to regard this case as a constitutional disease involving the kidneys, lymphatic system, brain, heart and respiratory tract. We were at first quite doubtful as to the diagnosis. We considered rheumatic fever, also tuberculosis and a vitamin deficiency.

While the child was on the ward, a case of a woman with acute disseminated lupus erythematosus was discussed at one of the clinicopathological conferences. She had had a definite rash and, among other symptoms, a pericarditis and cardiac involvement; the x-rays of the heart before and after the cardiac lesions became apparent were almost duplicates of those in this case. With this lead, and on re-evaluating the whole clinical course, we made a diagnosis of acute disseminated lupus erythematosus, in spite of the absence of a rash. Several weeks later and two days before the death of our patient, the typical rash appeared and clinched the clinical diagnosis.

Dr. Jacob Lerman: Dr. Higgins deserves the credit for making the diagnosis in this case after listening to a similar case report. On seeing the patient, at his request, I agreed with his diagnosis. This girl seemed to have all the visceral manifestations of the disease but no skin eruption. She had pericarditis, pleuritis and, I am certain, peritonitis as well. I obtained a history of joint pains before she came to the hospital, though her statements in regard to this symptom seem to have been somewhat contradictory, and when I saw her I thought she showed swelling of several joints. There was a history of nosebleeds and, on two occasions, petechiae were found on the palate, suggesting a hemorrhagic tendency. The anemia, leukopenia, and bouts of fever were quite characteristic. Her face was swollen but there was no venous engorgement or sufficient renal damage to account for it.

It is noteworthy that the blood cultures were repeatedly negative. Positive blood tests for syphilis were confusing. However, I have seen such positive tests in several similar instances. The tests were probably falsely positive because of some toxic substance in the blood.

Clinical Diagnoses

Acute disseminated lupus erythematosus.
Bronchopneumonia.

Dr. Hill's Diagnoses

Multiple abscesses of kidneys.
Empyema.

Dilatation of heart.
Septicemia, probably streptococcus.
Terminal pneumonia.

Anatomical Diagnoses

Acute disseminated lupus erythematosus.
Hydropericardium.
Empyema, left, hemolytic streptococcus.
Bronchopneumonia.
Septicemia, hemolytic streptococcus.

Pathological Discussion

Dr. Tracy B. Mallory: I, too, was given an opportunity of making a clinical diagnosis upon this patient a few weeks before her death but did not have the courage of Dr. Higgins and Dr. Lerman to make a diagnosis of acute disseminated lupus in the complete absence of a skin rash or the ingenuity of Dr. Hill to imagine a train of complications to pyelitis which would account for the diversified symptomatology. Dr. Higgins has, in this case, the advantage of having made a diagnosis which — as you may remember from the argument between Dr. Soma Weiss and me[1] at another of these conferences — the pathologist can do little either to prove or to disprove. Dr. Hill, on the other hand, has been rash enough to make common diagnoses, such as abscesses in the kidneys, purulent pleuritis and pneumonia. There was, as Dr. Hill predicted, bronchopneumonia, a terminal streptococcal septicemia and a purulent pleuritis, but I do not believe that they had been present long or accounted for very much of this child's story. A streptococcal infection of three months' duration would certainly have shown more findings and different findings from what we observed at autopsy. There were 400 cc. of quite clear fluid in the pericardium. The heart was of normal size. There was turbid fluid in the left chest which showed streptococcus on smear. Blood culture showed the same organism. The kidneys were grossly negative. On microscopic examination they showed only scattered foci of change in an occasional glomerulus, the type of lesion usually described as embolic nephritis.

This makes, I think, the fifteenth case of what we believe is this disease that has come to autopsy in this hospital, and in all these cases we have never been able to find any constant anatomic lesion. The skin lesion is probably the most constant of all, yet it comes and goes. This child's appeared two days before death. In other cases it occurs early and disappears weeks before the patient dies. The kidneys according to Baehr, Klemperer and Schifrin[2] should show in most cases a specific lesion of the glomerular tufts. We have been able to find it in only two of our cases though a nonspecific focal glomerulonephritis has been present in about half a dozen. The necropsies almost always show fluid in the pericardium. It is usually clear and looks like a transudate, not an exudate. The symptoms often suggest an endocarditis, and in two or three of our cases such a lesion has been present. The only diagnosis that can be inferred from the autopsy findings is the one made on the wards — acute disseminated lupus erythematosus.

Dr. R. Earle Glendy: Have any of the previously reported cases been diagnosed before the appearance of the skin lesions?

Dr. Mallory: In one case in this hospital a presumptive clinical diagnosis was made by Dr. Bauer in the absence of skin lesions. The autopsy was entirely negative except for effusions in the serous cavities — a finding which at least does not disprove the diagnosis.

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CASE 24342

Presentation of Case

First Admission. A forty-nine-year-old, white, married, Polish storekeeper entered the hospital with the complaint of pain in the joints of ten weeks' duration.

Fourteen weeks before entry the right side of his throat became sore and remained so up to the time of entry. Ten weeks before entry this symptom became more acute, and about that time he began to have pain in the right wrist unaccompanied by tenderness, redness, stiffness or swelling. In the course of the next few days he developed similar pain in his right wrist and shoulder, and a "gland" in front of his right ear became swollen. About seven weeks before entry he developed pain in his right hip, knee and ankle which was somewhat aggravated by walking. He consequently stopped working and stayed at home. He had no chills or fever but began to have occasional drenching night sweats, and he noticed that he was weaker than formerly. During the six weeks before entry his symptoms remained about the same except that he had less pain in his arm. Cold or damp weather increased his joint pain, but it was never severe enough to keep him from walking. Occasionally after coughing he had a brief stabbing pain in the right lower chest which radiated down the right flank and sometimes to the right testis. He had no dyspnea, orthopnea, persistent cough,

constricting sensation in the chest, palpitation or hemoptysis. He denied ever having had gonorrhea, syphilis, scarlet fever, rheumatic fever or chorea. He thought he had lost some weight during the few months before entry. His family history was negative except that two of his sons had died of sarcoma.

Physical examination revealed a well-developed, well-nourished man in no discomfort. There was injection of the throat, with some apparent tonsillitis. The heart and lungs were negative. The blood pressure was 150 systolic, 96 diastolic. There was a questionable, slightly tender mass in the right upper quadrant which was thought to be a palpable kidney. Rectal examination showed moderate enlargement of the prostate. There was slight tenderness of the right sacroiliac joint and of right iliolumbar and iliosacral ligaments. There was no limitation of motion or pain on motion.

The temperature was 98.6°F., the pulse 75. The respirations were 20.

The urine examination was negative. The blood showed a red-cell count of 5,430,000 with 90 per cent hemoglobin and a white-cell count of 7600 with 60 per cent polymorphonuclears. The nonprotein nitrogen of the blood was 28 mg. per cent, the uric acid 2.5 mg. per cent, the sedimentation rate normal, and a blood Hinton test negative. A gonococcus complement fixation test was negative, a throat culture gave no growth, and a smear of prostatic fluid showed no bacteria or pus cells. X-ray films of the right leg showed changes in the trabeculation of the upper end of the right tibia, which appeared only in the anteroposterior view. The right ankle was negative, and the bones around the right knee showed minimal arthritic changes, with no definite narrowing of the joint space. A film of the pelvis and hips showed no unusual changes for a patient of his age. There were slight changes around the crest of the right ilium.

He was discharged on the fourth day with the diagnosis of chronic tonsillitis, arthralgia and psychoneurosis.

Final Admission (three months later). For the first six weeks after discharge he felt poorly and suffered a good deal of pain in his right hip. He had no appetite and was unable to sleep. Finally his physician recommended tonsillectomy, which was done seven weeks before re-entry. Following the operation he had frequent hemorrhages from the operative site and remained in the outside hospital, where it was done, for eighteen days. On returning home he felt worse than before the operation and had a dull constant pain which involved the entire chest and shoulders. This pain persisted up to the time of re-entry. About one week before re-entry he noticed some swelling of the right foot, with a tender red cord running up his leg along the course of the saphenous vein. He had noticed enlarged lymph nodes in the right groin.

Physical examination revealed him to be still well nourished. During the examination he persistently caught his breath during expiration. Dullness, bronchial breathing and increased voice sounds were heard at the right apex, and there were a few rales at the right base. There were also slight clubbing and cyanosis of the fingertips. The heart and lungs were otherwise negative, and the abdomen was negative. The blood pressure was 140 systolic, 80 diastolic. He moved his right leg with difficulty, although it showed no weakness, atrophy or limitation of motion. There was a tender area in the region of the crest of the right ilium. The right inguinal lymph nodes were enlarged, and the right saphenous vein was tender and cord-like, with redness over the medial aspect of the calf. There was some edema of the right ankle and foot.

The temperature was 99.8°F., the pulse 100. The respirations were 25.

The urine examination was negative. The blood showed a red-cell count of 4,840,000 with 85 per cent hemoglobin and a white-cell count of 11,100 with 64 per cent polymorphonuclears. The guaiac test on the stool was negative, and the sedimentation rate was normal.

An x-ray of the pelvis showed a definite change since the last observation. There was mottled atrophy involving all bones. There was definite increase in the size of the right pubic ramus, without increase in the trabecular markings. Overlying the right ilium there was a ring shadow with sharply defined margins which appeared to be in the bone.

An x-ray film of the chest showed dullness occupying the region of the right upper and middle lobes. The diaphragm on that side was elevated, and the costophrenic angle was clear. The trachea was in the midline, and there was no definite evidence of shift of the mediastinum. The left lung was negative except for a somewhat low diaphragm. The heart shadow was somewhat prominent in the region of the left ventricle.

During his first seven days in the hospital his temperature fluctuated between 98 and 100°F., and three white counts varied between 10,000 and 20,000. On the eighth day he suddenly had acute respiratory distress. His blood pressure rose to 170 systolic, 110 diastolic, and he perspired freely. He had no acute pain, and there was no distention

of the neck veins. Breath sounds were diminished in the right lung and increased in the left. He gradually improved but two hours later had a similar episode and died.

Differential Diagnosis

Dr. Howard C. Coggeshall: Judging from the clinical data covering the first admission, it was thought that the patient complained of more symptoms than seemed to be justified by the physical findings.

As one reviews the history it seems apparent that most of the pain could be accounted for by nerve-root pain. Starting fourteen weeks prior to entry he had pain in the right side of the neck, which may have focused attention on the right tonsil. Within seven weeks this nerve-root pain involved the entire right side, neck, arm, chest, abdomen, testicle and leg. Occasionally when he coughed, pain radiated from the right chest into the right flank. No deductions can be made from the history of increased pain during damp weather.

The first physical examination was essentially negative except for a swollen "gland" in front of his right ear, a questionably palpable kidney, moderate hypertrophy of the prostate and tenderness over the right sacroiliac joint and ligaments. The description of the second examination three months later fails to mention any abnormality of the cervical "gland," the kidney or the prostate. Therefore, the significance of the abnormalities of these structures can be minimized, and I assume that the prostate did not enlarge during the interim. During these three months other gross physical changes occurred: an area of consolidation in the right apex, clubbing of the fingertips, inco-ordination of the voluntary movements of the right leg, a painful area over the crest of the right ilium, enlargement of the right inguinal lymph nodes, and a tender cord along the course of the right saphenous vein. I shall omit the roentgenological findings at this time. The sedimentation rate was normal, which was evidence against the condition's being due to an infection or a multiple myeloma. I do not believe that the tonsillitis, the tonsillectomy and the postoperative hemorrhage had any relation to the fatal disease process. One would like to know more about the time relation between the appearance of pain in the right chest and the thrombophlebitis of the right saphenous vein. This information would be helpful in deciding whether the right lung consolidation was a primary lesion or one due to infarction following pulmonary emboli. Thus far the clinical data have been negative for evidence of mucous-membrane hemorrhage, namely epistaxis, hemoptysis, hematemesis, hematuria or melena. In any malignant process involving the lungs, kidney or prostate one would expect to have some evidence of hemorrhage. I think it is quite obvious that this patient was suffering from carcinomatosis because of the following: rapid change in physical findings; short duration of the illness (six months); asymmetrical involvement; nerve-root pain; and roentgenological evidence of progressive bone destruction in the pelvis and an area of consolidation in the right upper and middle lung lobes. I believe that examination of the roentgenograms will be helpful in determining the primary site of the malignant growth.

Dr. Tracy B. Mallory: Unfortunately we have lost the roentgenograms and will have to rely on the interpretation in the record.

Dr. Coggeshall: Roentgenological examination of the pelvis showed mottled atrophy of all bones, a circumscribed area of diminished density in the right ilium and an increase in the size of the right pubic ramus. These changes took place within a three-month period. Roentgenograms of the chest showed an area of diminished density occupying the right upper and middle lobes of the lung. There was no evidence of a mediastinal shift, and the trachea was in the midline. These findings were consistent with a widespread carcinomatosis. The mass in the chest was either a malignant process or an infarct which resulted from an embolus arising in the right saphenous vein or the inferior vena cava. Without seeing the x-ray films of the chest I cannot be sure of what was in the right upper and middle lobes other than an area of consolidation, but with the evidence of metastatic involvement of the bones of the pelvis, there is no doubt that he had a malignant growth some place. The data at hand are not adequate to say whether the malignancy was a primary or secondary growth in the lung. Is there anything in the record concerning the roentgenologist's interpretation of the changes in the pubic ramus and chest?

Dr. Mallory: He said the pubic ramus showed periosteal reaction and a definite increase in size. He ruled out Paget's disease. He also said there was no increase in the thickness of the trabeculae. The dullness in the chest was interpreted as consolidation only. No statement was made about new-bone formation around the rarefied lesion in the ilium.

Dr. Coggeshall: The manner in which he died was strange. There must have been an obstructive lesion either in the pulmonary circulation or in the trachea. The sudden termination suggests pulmonary embolism with the embolus's coming from the saphenous vein or inferior vena

cava. There was no distention of the neck veins, acute chest pain, cough or sputum. However, the breath sounds did disappear. I do not believe a person could die of asphyxiation from a blocking of the trachea as quickly as was described in this instance. The increase of the blood pressure from 140 systolic, 80 diastolic to 170 systolic, 110 diastolic, must mean that there was some obstruction to circulation. I should put the immediate cause of death as pulmonary embolism. At first I thought the entire clinical picture could be explained on the basis of a primary pulmonary malignancy with metastatic involvement of the pelvic bones, but I am not willing to name the primary site without seeing the roentgenograms. I think one can only guess whether the primary lesion was in the lung, prostate or kidney. He probably had a carcinoma in spite of the family history telling us that two sons died of sarcoma: it would be unusual for a third member of the family to have the same disease. The primary lesion might be a lymphoma; the normal sedimentation rate rules out the possibility of multiple myeloma.

Dr. James H. Means: I should like to suggest that the terminal episode was cerebral rather than pulmonary because the blood pressure went up and there was no distention of the neck veins. He had dyspnea and perspired a great deal. A cerebral lesion could cause these symptoms and signs.

Dr. Mallory: We cannot answer that point, because the head was not examined.

Clinical Diagnoses

Primary carcinoma of the lung?
Metastatic carcinoma of bones of pelvis.
Phlebitis, saphenous vein.
Pulmonary embolism.

Dr. Coggeshall's Diagnoses

Carcinomatosis.
Primary lung carcinoma?
Pulmonary embolism.
Phlebitis, saphenous vein.

Anatomical Diagnoses

Carcinoma of lung, right upper lobe, with metastases to epicardium, bones and retroperitoneal lymph nodes.
Pulmonary atelectasis, right middle and lower.
Pleuritis, acute and chronic.
Tracheitis and bronchitis, acute.
Hydrothorax, right.
Pulmonary edema, left.
Hydropericardium.
Phlebitis of veins of right leg.

Pathological Discussion

Dr. Mallory: The man had widespread metastatic carcinoma, and the primary source was the lung or, more exactly, the right primary bronchus just at the point where the bronchus to the upper lobe branches off. A characteristic tumor nodule was present in the bronchial wall, had completely obliterated the lumen of the upper lobe bronchus, had narrowed the main bronchus, and had infiltrated extensively the upper lobe. Beyond the point of tumor involvement there was a fibrous pneumonitis, evidently the result of prolonged infection behind the point of obstruction. The middle and lower lobes were completely atelectatic, probably as the result of a large pleural effusion, but did not contain any tumor. The left lung showed an acute and massive pulmonary edema. There were no pulmonary emboli. The immediate mechanism of death, I take it, was anoxemia, since he had one completely atelectatic lung and the other drowned with edema fluid. The heart seemed normal, but the pericardium, both visceral and parietal, showed tumor infiltration and an effusion of 400 cc. The saphenous veins did contain a thrombus, but no emboli had developed from it. That in general is the rule: the saphenous vein is very rarely the source of any of the pulmonary emboli we find so often at autopsy. The bones were very extensively involved with metastatic tumor, and the adrenals, though grossly negative, showed microscopic metastases.

Dr. J. Wallace Zeller: It is said that he had slight clubbing of the fingers.

Dr. Mallory: It was the kind of clubbing about which there could be two opinions. We described it as an incurving of the nails without clubbing.

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THE SILLY SEASON

Hay as a merchantable commodity may have been relegated mainly to the rural regions, but haywire remains with us as the rather pathetic mainspring of the silly summer season. To what extent haywiriness is a natural and inevitable development of the dog days — a damp humor born of heat and humidity — is difficult to say. Undoubtedly weather and the slack season are behind this trend toward the twisted shackles of desiccated timothy, redtop and alfalfa, but there are other motivations.

We suspect that business might pursue its sane if somewhat humdrum way, were the perspiring pen-pushers of a bogged-down Fourth Estate not afflicted with the scabietic urge to make something out of nothing. It is interesting, but rather pitiful to note what putty we are in the hands of the penny-thriller purveyors. A preadolescent moving picture actress develops the sniffles in Boston; a physician must be rushed from Hollywood by plane. No reflection on the Boston doctors, you understand, but in the cinema business, if it doesn't cost money, it's no good, and a headline a day keeps the doldrums away.

A demented youth leaps tardily from a vertiginous altitude and sews up an entire front page, with photos; a "broth of a lad" illegally risks his life in a one-to-one-thousand gamble with the mechanical ingenuity of man and the North Atlantic weather, and he becomes the man of the hour, receiving the adulations of mayors, governors, ambassadors and what have you.

Even with no personal experience to guide us in the more remote zones of antiquity, we believe that the sweaty populace was always ready to clap its chopped hands and throw its hats into the air. Sensationalism has the greatest appeal, and the press of the country is making no high effort to direct the thoughts of the nation into inspiring or productive channels. The average citizen wants his news to be of about the same consistence as the pulp on which it is printed, with his taste perhaps at its lowest ebb in the beach-pajama season.

RENAL INFECTION AND HYPERTENSION

Several recent publications emphasize the relation of the history of renal infections, or of their presence at autopsy, to hypertension. The argument is further strengthened by reported cases — now appearing more frequently than in the past — of unilateral infectious lesions with hypertension that is cured by removal of the diseased kidney. The picture is further complicated by those who attribute pre-eclamptic and toxemic conditions in pregnancy to pyelitis. One author, Peters,[1] seems prepared to hold that toxemia, apart from pyelitis and some other conditions, should not be considered an entity, although something worthy of a name appears only in pregnant patients, some of whom have not had a history of renal infection or other infection at the time the toxic symptoms, accompanied by albuminuria

and hypertension, began. While admitting that "hypertension usually appears only after pyelonephritis has persisted for a long time and has destroyed a large part of both kidneys," Peters notes that "it would seem, then, that pregnancy contributes to pyelitis a peculiar and distinctive coloration with a propensity to explosions." He further states that "women who have pyelitis when pregnant seldom escape irreparable and enduring damage if the pregnancy is allowed to proceed." He must of necessity, and does, arrive at the conclusion that most cases of pyelitis in pregnancy should be interrupted.

The above view seems to be held chiefly in non-urological and non-obstetrical fields of medicine. There is an abundant literature on the end results of urinary-tract infections both in the pregnant and others, and considerable literature, in addition to unrecorded obstetrical and urological experience, to justify continuance in the present more conservative attitude toward infections and also toxemias. The Boston Lying-in Hospital can present cases of urinary tract infection in pregnancy which were severe enough to demand interruption and persisted uncured over periods ranging from eight to ten years, in which evidence of renal insufficiency or of hypertension has never occurred. The same clinic can also produce a considerable number of patients with toxemia or pyelitis who have recovered, passed through multiple succeeding pregnancies, and after a period of from twelve to sixteen years, still show neither renal insufficiency nor hypertension. Spontaneous recovery in the pyelitis of pregnancy does occur,[2] and some optimism is warranted in cases with toxemia.[3] In fact, at the clinic of this same hospital there are but three cases in which hypertension has developed where a *previous* diagnosis of hypertension or toxemia can be excluded. In all three there have been obstructive lesions present in the kidney or in the lower urinary tract. In one, the hypertension has been cured over a period of twelve years after nephrectomy on the occluded side. In this respect, these cases follow closely the findings in urological cases in which removal of the diseased kidney is followed by substantially reduced blood pressure. Most, if not all, of these cases, show obstructive lesions.

One assumes, then, that the wide divergence of opinion is based primarily on the source of material. An opinion which is founded on sick cases in hospitals and on autopsy material, to the exclusion of the literature which deals with recoveries, is bound to reflect pessimism.

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MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

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CASE HISTORY NO. 86. CENTRAL PLACENTA PREVIA

Mrs. J. B. C., a twenty-nine-year-old gravida III, entered the hospital March 18, 1936, with profuse painless bleeding.

The family history was negative. Her tonsils had been removed in childhood, and her appendix in 1928. Her two previous pregnancies had been normal. Catamenia began at twelve and had a regular twenty-eight-day interval; they lasted for five days, and she had experienced no difficulty until January, 1935. Since then she had had a great deal of dysmenorrhea. This was so marked that she came to the hospital for an examination. The uterus was found to be retroverted and could not be replaced. Three days after this examination catamenia began and were accompanied by intense pain at defecation and by some slight tenderness in both lower quadrants. A consultant was called, who made the diagnosis of endometriosis and advised laparotomy. On April 9, 1935, the abdomen was opened. The left ovary was studded with raspberry-like implants, as was the posterior wall of the uterus. There were two blood blisters on the posterior wall of the uterus which were the size of a thumbnail. These were resected and the left ovary was removed. The

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right ovary contained a recently ruptured graafian follicle. The uterus was suspended by the Olshausen technic. The convalescence was uneventful. Pregnancy was advised with the idea that it might cause a regression of the endometriomas. In the former she was successful, her last period being July 21, 1935, thus making her confinement expected April 28, 1936.

She was seen routinely during this pregnancy, and it progressed uneventfully until the time of her admission to the hospital because of a profuse flow of bright-red blood. The labor room and operating room were set up and ready on admission. Examination showed a pulse of 90; the uterus was soft, and the fetal heart present, and the child presented by the vertex, which was high. No vaginal examination was done, but a rectal examination showed the cervix not to be open. The amount of bleeding made immediate operation necessary. The softness of the uterus and the audible fetal heart precluded a complete separation of the placenta, and a presumptive diagnosis of partial previa, complete previa, or low-attached placenta was made. As the patient was not in labor, as the baby was viable and as the bleeding was profuse, abdominal section seemed to be the conservative operation even though she was a multipara.

Under nitrous oxide, oxygen and ether anesthesia a classical section was performed. A complete, centrally implanted placenta was found. The baby and placenta were delivered; the baby was in good condition. One thousand cubic centimeters of 5 per cent glucose was given subcutaneously, and the patient left the operating room with a pulse of 120 and a blood pressure of 110 systolic, 80 diastolic. The baby weighed 6 lb., 4 oz. Convalescence was uneventful.

Examination eight weeks later showed a well-healed abdominal wound and a uterus that was freely movable and anterior in position. There was no tenderness in either vault. Up to date there has been no return of dysmenorrhea.

Comment. This patient was apparently not grouped. Transfusion was not necessary, but routine grouping, as has been pointed out many times, is a necessary procedure.

There are many cases of endometriosis in the literature in which the patient has become pregnant following operation: this is another case in point. Undoubtedly some will criticize a cesarean section on a multipara at eight months, but the amount of bleeding made operation imperative, and the viability of the child is best guaranteed by this treatment. The outcome justified the procedure.

OBITUARIES

KALLMAN MEYER DAVIDSON

1862 - 1938

With the death of Kallman Meyer Davidson in his seventy-sixth year, on July 22, 1938, there passed from our midst a striking personality embodying qualities which give a place of honor to the family physician. Cultured, keeping zealously abreast with medical progress, endowed with a good stock of common sense and a fine sense of humor, he was the beloved adviser of three generations.

He had been in active medical practice for over half a century, and since 1891 here in Boston. He brought to our community at that time a combination of the best in Russian-Jewish culture with the thorough training in medicine afforded in Germany in the last quarter of the nineteenth century, under the direct influence of men like Hermann, Virchow, Koch, Ehrlich, Naunyn and Minkowski. Thus prepared and with a naturally keen and inquisitive mind he was from the first a pioneer in raising the standards of medical practice especially among the immigrant part of our population. This was recognized not only by the people he served but also by the leaders of the profession, as shown by the friendship in those days of such men as Frederick C. Shattuck, Maurice H. Richardson and Reginald H. Fitz.

Particularly noteworthy was his active leadership in developing hospital service among his people here in Boston. In 1903 he was the prime mover in the organization of the Mount Sinai Dispensary, and in 1913 he was a leader in the founding of the Beth Israel Hospital, which has since developed into an outstanding institution.

Doctor Davidson was an indefatigable worker and always considered the practice of medicine as clinical research. He loved books and read extensively the medical literature. Ever young in spirit and in his interests he was a familiar figure at medical gatherings, and found great pleasure in his membership in the American College of Physicians.

He was a man of great fortitude and bore most courageously two calamities in his life — the loss of his beloved wife and more recently the untimely death of his brilliant son, Dr. Percy B. Davidson.

His memory will long be cherished.

H. M.

HOMER GAGE

1861 - 1938

Homer Gage, born in Worcester, October 18, 1861, died from a heart attack at his country place in Shrewsbury, July 3, at the age of seventy-seven.

The son of Dr. Thomas H. Gage, a former president of the Massachusetts Medical Society and for many years a leader in medical affairs in central Massachusetts, he graduated from Worcester High School, received his A.B. from Harvard in 1882, his A.M. (magna cum laude) in 1883 and his M.D. in 1887. One of the most widely known among the medical practitioners of central Massachusetts, a surgical specialist for most of the thirty-five years during which he was engaged in the practice of medicine, he was, during the latter part of his life, as well known in philanthropic and business circles as he was to those more concerned with medical matters.

After service as surgical intern at the Massachusetts General Hospital, he opened his office in Worcester on July 1, 1888, and was at once made one of the two gynecologists at the Washburn Free Dispensary and one of the three visiting surgeons to the Department of Children at the Memorial Hospital, opened but a few days earlier. In 1889 he was appointed assistant obstetrician to the Worcester City Hospital and in 1890 one of the surgeons to that institution. The latter position he held for twenty-seven years, resigning only to enter military service in 1917, at which time he was placed on the consulting staff, a position held at the time of his death. He was president of the staff of the Worcester City Hospital from 1905 until his resignation from active work. With the Memorial Hospital he was connected for fifty years almost to a day, successively as surgeon, surgeon-in-chief, — a position created especially for him, — consulting surgeon, trustee, vice-president and finally, in 1929, president of the board. He became one of the visiting surgeons to St. Vincent's Hospital at the time of its foundation in 1894 and on his resignation from active service, fourteen years later, was retained as a consultant during the remainder of his life.

He was a fellow of the American Surgical Association, serving as vice-president in 1919, and a fellow of the New England Surgical Association, being president in 1923. He was also a fellow of the American College of Surgeons. For forty-eight years he was a councilor of the Massachusetts Medical Society, serving as a member of the Committee on Membership and Finance from 1919 to 1929 and of the Committee on Publications from 1928 to 1936, being chairman of the latter for the first five years of his term.

A lieutenant in the Medical Reserve Corps of the United States Army, Dr. Gage in November, 1917, was ordered to Camp Devens, where within a few weeks he was advanced to the rank of major and placed in charge of the surgical division of the Base Hospital. He held this position until February, 1919, when he was retired from active duty with the rank of lieutenant-colonel. He was a member of the Military Order of the World War and of the American Legion and in 1929 served as commander of Worcester Post 5 in the latter organization.

His interest in life insurance made him medical director of the State Mutual Life Insurance Company and president in 1917 of the Life Insurance Medical Directors Association. At the time of his death, he was a consultant to the Medical Department of the former, a director and a member of the Executive Committee.

In 1907 he became a member of the Board of Trustees of the Worcester Polytechnic Institute and in 1911 was elected treasurer. In 1929 the honorary degree of Doctor of Engineering was conferred upon him by this institution. In 1921 he became a member of the Board of Overseers of Harvard University, and in 1928 was re-elected for a second term. During these years he served as a member of the Executive Committee, as chairman of the Committee on Honorary Degrees, and on the committee to visit the Harvard Medical School and the Graduate School of Arts and Sciences.

In 1921 Dr. Gage was elected president of the Worcester Welfare Association and until his death was annually re-elected to that position. Yearly, under his guidance, the sums needed for the work of the leading charitable organizations of Worcester were raised, and in 1929, at a testimonial dinner, the campaign captains honored him with the following testimonial:

> In the love of mankind and in the service of your fellow men you have given of yourself with a fine full measure of devotion that has endeared you to everyone in every walk of life.
>
> We feel that your greatest satisfaction has been in bringing help to the weak, light where there was darkness, hope where there was despair.
>
> Your only reward has been the satisfaction of a work well done. You ask no other.
>
> We express tribute, love and appreciation to you for distinguished and unselfish devotion to a great and noble duty, and we ask for no greater honor and privilege than to serve under you in the years to come.

A director of the Crompton and Knowles Loom Works since 1900, in 1920 he was elected president

of the company on the death of his brother-in-law, Lucius J. Knowles. This position he held at the time of his death. He was a director of the Old Colony Trust Company and of the First National Bank, of Boston, of the Worcester County Trust Company and of several mercantile associations and a trustee of the Worcester County Institution for Savings.

The extent of the various activities of this man was really remarkable, as was the ability with which he discharged the duties of his various positions, retaining in each one of them not only the admiration but the affection of those with whom he worked.

No social or civil service appealed to him in vain. His ability to persuade others to contribute to various important projects was really phenomenal and he seemed never to tire of well-doing. Contributions of money, of time and of labor were given willingly and generously by both Dr. and Mrs. Gage to every movement for social improvement in his native city.

The honor accorded his memory at a memorial service held in the American Cathedral soon after his death was a tribute to the work of both Dr. and Mrs. Gage in connection with the national dormitories of the University of Paris. Seven years after a wealthy Frenchman had provided 10,000,000 francs as the nucleus for the general project, no money had been given to erect the American dormitory. Dr. Gage became at this time chairman of a committee to raise the needed $400,000, and in three years, by his efforts, the money was obtained and the building erected and dedicated at a ceremony honored by the presence, among others, of the President of the French Republic. Dr. Gage had been made an officer of the Legion of Honor and in 1930 was promoted to the rank of commander. The memorial service was attended by the United States Ambassador, by the French Minister of Finance, the Rector of the University of Paris, the Minister of Foreign Affairs and some three hundred distinguished individuals, many of whose names are well known not only in France but in this and other countries. F. W. Beekman, dean of the cathedral, told of Dr. Gage's professional, charitable, philanthropic and public work, of his many honors, of his breadth of vision and of the universality of his interests, not forgetting what both he and Mrs. Gage had done in France before the United States entered the World War.

On June 15, 1893, Dr. Gage married Miss Mabel Reynolds Knowles, who survives him. Their son and only child, Homer Gage, Jr., a veteran of the World War who saw active service in France, died unmarried in 1927.

S. B. W.

MISCELLANY

REGULATIONS ON NEW FOOD, DRUG AND COSMETIC ACT

M. L. Wilson, Acting Secretary of Agriculture, has approved and promulgated regulations for the administration and enforcement of certain provisions of the recently enacted Federal Food, Drug and Cosmetic Act. These regulations — which cover Sections 201 *(p)*, 505, and 702 of the new law — relate to provisions of the act that became effective immediately upon its approval on June 25, 1938. Under these provisions dangerous drugs, injurious cosmetics, and inadequately tested new drugs are denied the channels of interstate distribution.

Because enforcement operations require that these regulations be made effective at the earliest possible date, their issuance has not been delayed until hearings could be held upon them. But department officials said that they will welcome constructive suggestions as to necessary revisions. Upon the basis of such suggestions proposed revisions will be announced as soon as possible and dates and places for public hearings will be fixed, notwithstanding the fact that the statute does not specifically require such hearings.

In addition to these regulations, other necessary regulations relating to the immediate effective provisions of the law will be issued as soon as practicable. These will include import regulations and those covering the conduct of hearings. The adoption, for the purposes of the new law, of the import regulations now effective under the old Food and Drugs Act of 1906, is being proposed to the Secretary of the Treasury. Regulations governing the conduct of hearings are being formulated.

REGULATION UNDER SECTION 201 *(p)*

A drug may be a new drug by reason of: (1) the newness for drug use of any substance which composes the drug, in whole or in part, whether it be an active substance or a menstruum, excipient, carrier, coating or other component; (2) the newness for drug use of a combination of two or more substances, none of which is a new drug; (3) the newness for drug use of the proportions of the substances in a combination, even though the substances in certain other proportions do not constitute a new drug; or (4) the newness of the dosage, or methods or duration of administration or application, or other conditions of use of the drug prescribed, recommended, or suggested in the labeling thereof, even though the drug is not a new drug when used in certain different dosage, or in different methods or duration of administration or application, or in conditions that are otherwise different.

REGULATIONS UNDER SECTION 505

Subsection (a). A new drug shall not be deemed to be subject to Section 505 of the act if it is subject to the Virus, Serum and Toxin Act of July 1, 1902 (U.S.C., 1934 ed., Title 42, Ch. 4), or the Virus, Serums, Toxins, Antitoxins and Analogous Products Act of March 4, 1913 (U.S.C., 1934 ed., Title 21, Ch. 5), and complies with such act.

Subsection (b). To be valid an application must contain as a part thereof all the matter required by Section 505 (b) of the act; the Secretary shall not permit the filing of an application which is incomplete. The Food and Drug Administration shall notify the applicant of the date on which his application is filed.

Subsection (c). If the Secretary finds, before the date prescribed by Section 505 (c) of the act for an application to become effective, that he has no cause to issue an order under Section 505 (d) of the act refusing to permit the

application to become effective, the Food and Drug Administration shall so notify the applicant in writing, and the application shall become effective on the date of the notification.

Subsection (i). A new drug intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety of drugs shall be exempt from the operation of Section 505 of the act: (1) if its labeling bears the statement "for investigational use only;" (2) if it is delivered only to such experts and is used by them solely for investigation; (3) if each expert has adequate facilities for the investigation to be conducted by him; and (4) if the person who introduced the drug in interstate commerce, or delivered it for such introduction, holds a signed statement from each expert to the effect that he will not use the drug otherwise than in the investigation to be conducted by him unless and until an application under Section 505 (b) of the act becomes effective with respect to such drug.

REGULATIONS UNDER SECTION 702 *(b)*

(*a*) An official sample is a sample collected by an officer or employee of the department from a shipment or other lot of an article within the jurisdiction of the act, with records or other evidence showing such jurisdiction. Analysis includes examinations and tests.

(*b*) An official sample of a food, drug or cosmetic collected for analysis under the act shall be at least twice the quantity estimated by the officer or employee to be sufficient therefor, unless (1) the amount of the article available and reasonably accessible for sampling is less than twice the quantity so estimated, (2) the cost of twice the quantity so estimated exceeds $10, (3) the article is perishable, (4) the sample is collected from a shipment which is being imported or offered for import into the United States, or from a person named on the label of the article, or his agent, and such person is also the owner of the article or (5) the analysis consists principally of rapid analytical procedures, organoleptic examination, or other field inspection examinations or tests, made at the place where the sample is collected or in a mobile or temporary laboratory. In addition to the quantity of sample prescribed above the officer or employee shall, if practicable, collect as part of the sample such further amount of the article as he estimates to be sufficient for use as exhibits in the trial of any case under the act based on the sample.

(*c*) After the Food and Drug Administration has completed such analysis of an official sample of a food, drug or cosmetic as it determines, in the course of analysis and interpretation of analytical results, to be adequate to establish the respects, if any, in which the article is in violation of the act, and has reserved an amount of the article it estimates to be adequate for use as exhibits in the trial of any case under the act based on the sample, a part of the sample, if any remains available, shall be provided for analysis, upon written request, by any person named on the label of the article, or the owner thereof, or the attorney or agent of such person or owner, except when (1) the sample, after collection, has become decomposed or otherwise unfit for analysis or (2) the request is not made within a reasonable time before the trial of any case under the act based on the sample. The person, owner, attorney or agent who requests the part of sample shall specify the amount desired and make advance payment of the cost thereof. A request from an owner shall be accompanied by a showing of ownership, and a request from an attorney or agent by a showing of authority from such person or owner to receive the part of sample. When two or more requests for parts of the same sample are received the requests will be complied with in the order in which they were received so long as any part of the sample remains available therefor.

(*d*) When an official sample of a food, drug or cosmetic is the basis of a notice of hearing under Section 305 of the act, or of a case under the act, and the person who received the notice or who is a party to the case has no right under Paragraph (*c*) to a part of the sample, such person or his attorney or agent may obtain a part of the sample upon request accompanied by a statement from each person named on the label of the article, and owner thereof, who has not exercised his right under Paragraph (*c*), waiving such right. The operation of this paragraph shall be subject to the exceptions, terms and conditions prescribed in Paragraph (*c*). — *United States Department of Agriculture.*

THE BOSTON DISPENSARY

An increase of more than 800 per cent in the past ten years is the record of the Boston Dispensary's home medical service, according to the annual report recently issued in leaflet form.

The dispensary's district doctors paid 44,007 free visits during 1937 to the homes of Boston's needy sick as compared with 4724 calls in 1927. Last year, home visits cost the dispensary, a member of the Community Federation, about 78 cents each, it is pointed out.

"This service covers nearly all of Boston and is available to all who are ill in bed and unable to employ a physician," Frank E. Wing, director, explained. "Upwards of two thirds of the 22,736 patients cared for in 1937 were welfare cases. By applying free medical care the dispensary is saving the City of Boston, at rates prevailing in other communities, not less than $85,000 a year."

The report shows an increase during the past decade of 44.5 per cent in the morning clinic service — for those who pay little or nothing — and 133,646 visits last year as against 92,439 in 1927. Attendance in the evening clinics — for working people of small means — fell off 18.9 per cent last year, largely due to loss of jobs and the resulting transfer of patients to the morning service. There were 32,892 patients in the Monday, Wednesday and Friday evening clinics.

Heavier demands were made upon practically all the dispensary's major clinics during 1937, according to the report: ". . . on the one hand, by increasing numbers of patients caught without employment by the business recession; on the other hand, by the urge of the staff toward finer and more searching medical technic. WPA workers temporarily off relief, people otherwise self-supporting, without surplus earnings to pay doctors' bills, welfare recipients requiring medical care in their homes — these constituted the bulk of the heaviest load in our history which we have been called upon to carry."

The effectiveness of the dispensary's service has been steadily improving during the past decade, it is explained, by the adoption of more intricate and more costly procedures: by the application of new technics, as in allergy, endocrinology and x-ray and ultra-short wave therapy; active participation in the campaigns against cancer, heart disease and social diseases; further exploration in the field of psychiatry; and the consequent utilization of the departments of social service, nursing, nutrition and health education.

Through the generosity of the Bingham Associates Fund, the dispensary's new Joseph H. Pratt Diagnostic Hospital on Bennet Street will be opened in the fall, it is announced. At present, only 20 patients can be accom-

modated for study or short-time specialized treatment by a large and especially trained personnel. Of the 822 admissions during 1937, 514, or 64 per cent, were from outside Boston and in most cases were referred by general practitioners in relatively small communities for diagnosis of obscure medical problems. The new hospital will have 65 beds and improved facilities.

CORRESPONDENCE

STATE MEDICINE

To the Editor: I should like to comment on your editorial entitled "The National Health Problem." You speak of the "aroused public" which is nothing more than New Deal propaganda. The great majority of the people, from what I can ascertain, are not in favor of state medicine.

The writer made a study of this subject for a state medical society in 1917 and 1918. At that time an effort was made to introduce bills into several legislatures, setting up such a system. The American Association for Labor Legislation, a radical organization, was back of it. A so-called model bill was introduced, specifying that all people working for wages of $100 a month or less should be insured.

The proponents contended that sickness was the cause of poverty, whereas poverty very often causes illness. At that time actual statistics showed that a loss of less than 3 per cent was due to illness.

The great majority of the middle class of people of the United States own automobiles, radios and electric refrigerators, and spend money liberally for most everything imaginable, and the records show that the wage earners are the largest depositors in the banks of this country. To say that most of these people are unable to pay doctors and hospital bills is certainly ridiculous.

The interference in business by the New Deal, the wild experiments, destruction in the time of plenty and the spending of billions of dollars have reduced America to the low economic level of the present.

The medical profession is in no way to blame for this, and the implication by cheap magazines and some members of the profession that the doctors are incompetent is very far from the truth.

Medical education has been on a very high plane in this country for many years. About 95 per cent of all the medical colleges have been in Class A for years. The doctors graduating have served internships of from one to three years and are fully capable of practicing. Knowledge and skill are not concentrated in Boston or New York but are quite universal throughout the United States.

People die in America as well as elsewhere from child birth and surgical diseases, and all children do not get the proper food and care which is no fault of the medical fraternity. It is primarily an economic question as it always has been. Given the proper wages and income, the people can pay for medical attention without calling in a government agent when they are sick.

Any system that ruins a great independent profession like medicine is of no benefit to the public. The better type of men would not study medicine in the future. To spend years of study and several thousands of dollars and then be under government regulation would not be to the liking of the young men of America.

From time immemorial doctors have treated poor and deserving people for nothing; also many others who in time of financial trouble could not take care of the expense of an illness. No profession has ever done so much for humanity.

Conditions differ greatly in the various states. The problem is not the same everywhere. It is possible that some states may have to work out a plan to assist the low-income group.

The people are heavily taxed now, and I feel sure that a large proportion of them are against further taxation. The Government pay roll is now enormous and the addition of more employees would cause a greater burden on the middle class of people.

The profession as well as the public is dependent on good business conditions and prosperity. That is what we need. State medicine is one of the New Deal plans for complete socialization of America.

FRANK E. ROWE, M.D.

61 Pleasant Street,
Revere, Massachusetts.

* * *

Nor is the *Journal* in favor of state medicine. — Ed.

A CORRECTION

To the Editor: Experiments performed on rats and rabbits during the past several years had led to the conclusion that large doses of insulin create a constitutional condition of true hyperinsulinism, which may be fatal. The conclusion was so stated in the original copy of my recently published paper (Tolerance to and toxicity of insulin. I. With spontaneous eating. New Eng. J. Med. *219:* 77-83, 1938). In a recent extension of this work to cats, the first few experiments appeared to modify the former conclusion, which therefore was changed shortly before publication. The modified conclusion stated that the prolonged action of large subcutaneous doses of insulin is due partly to true hyperinsulinism and partly to retention of unabsorbed insulin at the injection site. Further experiments, in collaboration with Dr. C. A. Vicens, have shown an error in the first observations on cats and have resulted in a complete confirmation of the previous work. When large doses, for example 1000 units, of insulin are injected in the leg of a cat, and amputation performed after twelve or twenty-four hours, the insulin effect is not terminated or lessened but may continue for as long as forty-eight hours. The action in the amputation animals may even be slightly increased by the shock. The actual fact therefore is that a state of hyperinsulinism can be maintained for two days or more after the complete absorption of a subcutaneously injected dose.

FREDERICK M. ALLEN, M.D.

1031 Fifth Avenue,
New York City.

LICENSE REVOKED

To the Editor: The license of Dr. David H. Shulman, 481 Beacon Street, Boston, Massachusetts, was revoked by this Board on August 18, 1938, because of gross professional misconduct in connection with the care of a premature termination of pregnancy.

STEPHEN RUSHMORE, M.D., *Secretary,*
Board of Registration in Medicine.

State House,
Boston.

NOTICES

PSYCHIATRIC ROUNDS, BOSTON CITY HOSPITAL

For the rest of this year every Thursday morning at 10:30 psychiatric rounds, conducted by Dr. Merrill Moore, will be held on the Neurological Service at the Boston City Hospital.

These rounds are open to any physician or interested person. The dates on which they will be held are: September 1, 8, 15, 22, 29, October 6, 13, 20, 27, November 3, 10, 17, 24, December 1, 8, 15, 22, 29.

The rounds will start at Room 916 on the ninth floor of the Medical Building.

CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Orthopedic Consultant
Lowell	September 2	Albert H. Brewster
Salem	September 6	Harold C. Bean
Haverhill	September 7	Arthur T. Legg
Brockton	September 8	George W. Van Gorder
Gardner	September 13	Mark H. Rogers
Worcester	September 16	John W. O'Meara
Pittsfield	September 19	Francis A. Slowick
Springfield	September 21	Garry deN. Hough, Jr.
Fall River	September 26	Eugene A. McCarthy
Hyannis	September 27	Paul L. Norton

INACTIVE STATUS TRAINING COURSE

The tenth annual Inactive Status Training Course for medical-department reservists of the United States Army and Navy will be held at the Mayo Foundation, Rochester, Minnesota, October 3 to 15.

During the past nine years this school, the first of its kind, has been remarkably successful. Officers attending have been most enthusiastic. The general plan of former years will be followed. Special work in clinics and hospitals will be offered during the morning hours for those asking special assignments. Presentations of carefully selected subjects in military medicine are scheduled for the morning, afternoon and evening hours. There will be appropriate sections or special courses for officers of the Dental and Veterinary corps.

The school program for the last three days of the meeting, that is, October 13, 14 and 15, is merged with that of the Association of Military Surgeons of the United States. The Surgeons General of the United States Army, the United States Navy, and the United States Public Health Service will attend and participate. Outstanding medical officers from other nations will attend. The commanding generals of both the Sixth and Seventh Corps areas have signified their intention of being present.

All medical-department reservists are eligible for enrollment. Approved applicants will be enrolled upon the recommendation of the Surgeon of the Seventh Corps Area or the Surgeon of the Ninth Naval District. Applications should be made at an early date and should be forwarded through the respective reserve headquarters of the officer concerned.

REMOVAL

Charles R. Morgan, M.D., announces the removal of his office to 96 Bay State Road, Boston, on September 1. Telephone Kenmore 4029.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, August 29

Tuesday, August 30

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

Friday, September 2

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

Saturday, September 3

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Marshall N. Fulton.

*Open to the medical profession.

September 12-14 — American Association for the Study of Goiter. Page 545, issue of March 24, and page 145, issue of July 28.

September 12-15 — American Congress of Physical Therapy. Page 946, issue of June 2.

September 19-22 — Congress of the International Society of Surgery. Page 180, issue of August 4.

September 19-23 — American Association of Railway Surgeons. Page 181, issue of August 4.

September 26 and 27 — Symposium on Occupational Disease. Page 145, issue of July 28.

October 3-15 — Inactive Status Training Course. Notice above.

October 7 and 8 — Conference on Rural Medicine. Page 180, issue of August 4.

October 8 and November 15 — American Board of Ophthalmology. Page 282, issue of February 10.

October 17 and February 20, 1939 — American Board of Internal Medicine, Inc. Page 216, issue of August 11.

October 17-21 — Clinical Congress of the American College of Surgeons, New York City.

October 24-26 — Academy of Physical Medicine, Scientific Session. Washington, D. C.

October 24 - November 4 — Graduate Fortnight of the New York Academy of Medicine. Page 181, issue of August 4.

November 5 — American Board of Obstetrics and Gynecology. Page 145, issue of July 28.

March 27-31, 1939 — American College of Physicians. Page 36, issue of July 7.

BOOK REVIEWS

Demonstrations of Physical Signs in Clinical Surgery. Hamilton Bailey. Sixth edition, revised. 284 pp. Baltimore: William Wood & Company, 1937. $6.50.

This surgical text should be in the hands of every surgeon and of every practitioner who pretends to make surgical physical examinations. One cannot turn a page without finding something that will help out in a perplexing case. The book is of more value to the man in practice than to the student who knows, or thinks he knows, all the short cuts to diagnosis, but even the latter may profit by reading this new edition.

Any text which reaches its sixth edition within ten years of its first has declared its worth and popularity more convincingly than could the most praising reviewer. If the reviewer can merely call attention to this volume, whose value in this part of the world has apparently not been fully appreciated, he will have accomplished something of benefit.

Tuberculosis Hospital and Sanatorium Directory: A directory of sanatoria, preventoria, and general hospitals having departments for tuberculosis patients. 168 pp. New York: National Tuberculosis Association, 1938. $1.00.

This is a useful directory of 749 institutions for tuberculosis patients in the United States, Alaska, Hawaii, Puerto Rico and the Philippine Islands. It covers federal, state, county, municipal, private and semi-private hospitals, with details in regard to each. There is a good index.